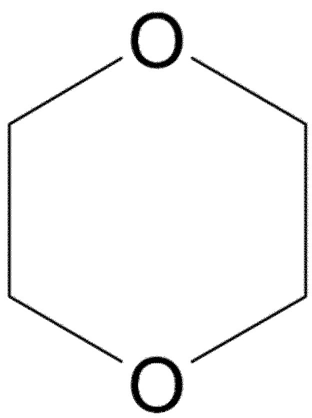
EPA Document# EPA-740-R1-7003
June 2017
Office of Chemical Safety and
Pollution Prevention

United States
Environmental Protection Agency

# Scope of the Risk Evaluation for 1,4-Dioxane

## CASRN: 123-91-1




*June 2017*

# TABLE OF CONTENTS

## LIST OF TABLES



## LIST OF FIGURES



## LIST OF APPENDIX TABLES



## LIST OF APPENDIX FIGURES

# ACKNOWLEDGEMENTS

This report was developed by the United States Environmental Protection Agency (U.S. EPA), Office of Chemical Safety and Pollution Prevention (OCSPP), Office of Pollution Prevention and Toxics (OPPT).

**Acknowledgements**

The OPPT Assessment Team gratefully acknowledges participation or input from EPA's Office of General Counsel, Office of Research and Development and assistance from EPA contractors CSRA LLC (Contract No. CIO-SP3, HHSN316201200013W), ERG (Contract No. EP-W-12-006), ICF (Contract No. EP-C-14-001) and SRC (Contract No. EP-W-12-003).

**Docket**

Supporting information can be found in public docket: EPA-HQ-OPPT-2016-0723.

**Disclaimer**

# ABBREVIATIONS

| | |
|---|---|
| °C | Degrees Celsius |
| AAL | Allowable Ambient Level |
| ACGIH | American Conference of Government Industrial Hygienists |
| AEGL | Acute Exposure Guideline Level |
| AES | Alkyl Ethyl Sulphates |
| AQS | Air Quality System |
| atm | Atmosphere(s) |
| ATSDR | Agency for Toxic Substances and Disease Registries |
| BAF | Bioaccumulation Factor |
| BCF | Bioconcentration Factor |
| BSER | Best System of Emission Reduction |
| CAA | Clean Air Act |
| CASRN | Chemical Abstracts Service Registry Number |
| CBI | Confidential Business Information |
| CCL | Candidate Contaminant List |
| CDR | Chemical Data Reporting |
| CERCLA | Comprehensive Environmental Response, Compensation and Liability Act |
| $cm^3$ | Cubic Centimeter(s) |
| COC | Concentration of Concern |
| cP | Centipoise |
| CPCat | Chemical and Product Categories |
| CSCL | Chemical Substances Control Law |
| EC | European Commission |
| EPA | Environmental Protection Agency |
| EPCRA | Emergency Planning and Community Right-to-Know Act |
| EU | European Union |
| FDA | Food and Drug Administration |
| FFDCA | Federal Food, Drug and Cosmetic Act |
| g | Gram(s) |
| GACT | Generally Available Control Technology |
| HAP | Hazardous Air Pollutant |
| HPV | High Production Volume |
| IARC | International Agency for Research on Cancer |
| IRIS | Integrated Risk Information System |
| ISHA | Industrial Safety and Health Act |
| kg | Kilogram(s) |
| kPa | Kilopascal(s) |
| L | Liter(s) |
| lb | Pound |
| Log $K_{oc}$ | Logarithmic Soil Organic Carbon:Water Partitioning Coefficient |
| Log $K_{ow}$ | Logarithmic Octanol:Water Partition Coefficient |
| $m^3$ | Cubic Meter(s) |
| MACT | Maximum Achievable Control Technology |
| mg | Milligram(s) |

| | |
|---|---|
| µg | Microgram(s) |
| mmHg | Millimeter(s) of Mercury |
| MSDS | Material Safety Data Sheet |
| NAC | National Advisory Committee |
| NAICS | North American Industry Classification System |
| NATA | National Air Toxics Assessment |
| NCEA | National Center for Environmental Assessment |
| NEI | National Emissions Inventory |
| NESHAP | National Emission Standards for Hazardous Air Pollutants |
| NICNAS | National Industrial Chemicals Notification and Assessment Scheme |
| NIH | National Institute of Health |
| NIOSH | National Institute of Occupational Safety and Health |
| NOAEL | No-Observed-Adverse-Effect Level |
| NPRI | National Pollutant Release Inventory |
| NSPS | New Source Performance Standards |
| NTP | National Toxicology Program |
| OCSPP | Office of Chemical Safety and Pollution Prevention |
| OECD | Organisation for Economic Co-operation and Development |
| OPPT | Office of Pollution Prevention and Toxics |
| OSHA | Occupational Safety and Health Administration |
| PBPK | Physiologically Based Pharmacokinetic |
| PEL | Permissible Exposure Limit |
| PET | Polyethylene Terephthalate |
| POD | Point of Departure |
| POTW | Publicly Owned Treatment Works |
| ppm | Part(s) per Million |
| PWS | Public Water System |
| RCRA | Resource Conservation and Recovery Act |
| REL | Recommended Exposure Level |
| SDS | Safety Data Sheet |
| SDWA | Safe Drinking Water Act |
| SIDS | Screening Information Data Set |
| TCA | 1,1,1-Trichloroethane |
| TCCR | Transparent, Clear, Consistent and Reasonable |
| TLV | Threshold Limit Value |
| TRI | Toxics Release Inventory |
| TSCA | Toxic Substances Control Act |
| TWA | Time-Weighted Average |
| UCMR | Unregulated Contaminant Monitoring Rule |
| U.S. | United States |
| UV | Ultraviolet |
| VCCEP | Voluntary Children's Chemical Evaluation Program |
| VOC | Volatile Organic Compound |
| WHO | World Health Organisation |

# EXECUTIVE SUMMARY

TSCA § 6(b)(4) requires the United States Environmental Protection Agency (U.S. EPA) to establish a risk evaluation process. In performing risk evaluations for existing chemicals, EPA is directed to "determine whether a chemical substance presents an unreasonable risk of injury to health or the environment, without consideration of costs or other non-risk factors, including an unreasonable risk to a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation by the Administrator under the conditions of use." In December of 2016, EPA published a list of 10 chemical substances that are the subject of the Agency's initial chemical risk evaluations (81 FR 91927), as required by TSCA § 6(b)(2)(A). 1,4-Dioxane was one of these chemicals.

TSCA § 6(b)(4)(D) requires that EPA publish the scope of the risk evaluation to be conducted, including the hazards, exposures, conditions of use and potentially exposed or susceptible subpopulations that the Administrator expects to consider. This document fulfills the TSCA § 6(b)(4)(D) requirement for 1,4-dioxane.

This document presents the scope of the risk evaluation to be conducted for 1,4-dioxane. If a hazard, exposure, condition of use or potentially exposed or susceptible subpopulation has not been discussed, EPA, at this point in time, is not intending to include it in the scope of the risk evaluation. As per the rulemaking, Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act (TSCA), with respect to conditions of use in conducting a risk evaluation under TSCA, EPA will first identify "circumstances" that constitute "conditions of use" for each chemical. While EPA interprets this as largely a factual determination—i.e., EPA is to determine whether a chemical substance is actually involved in one or more of the activities listed in the definition—the determination will inevitably involve the exercise of some discretion.

In the case of 1,4-dioxane, EPA anticipates that production of 1,4-dioxane as a by-product from ethoxylation of other chemicals and presence as a contaminant in industrial, commercial and consumer products will be excluded from the scope of the risk evaluation. These 1,4-dioxane activities will be considered in the scope of the risk evaluation for ethoxylated chemicals. EPA believes its regulatory tools under TSCA section 6(a) are better suited to addressing any unreasonable risks that might arise from these activities through regulation of the activities that generate 1,4-dioxane as an impurity or cause it to be present as a contaminant than they are to addressing them through direct regulation of 1,4-dioxane.

To the extent practicable, EPA has aligned this scope document with the approach set forth in the risk evaluation process rule; however, the scope documents for the first 10 chemicals in the risk evaluation process differ from the scope documents that EPA anticipates publishing in the future. Time constraints have resulted in scope documents for the first 10 chemicals that are not as refined or specific as future scope documents are anticipated to be.

Because there was insufficient time for EPA to provide an opportunity for comment on a draft of this scope document, as it intends to do for future scope documents, EPA will publish and take public comment on a problem formulation document which will refine the current scope, as an additional interim step, prior to publication of the draft risk evaluation for 1,4-dioxane. This problem formulation is expected to be released within approximately 6 months of publication of the scope.

In 2015, EPA/OPPT published a *Problem Formulation and Initial Assessment for 1,4-Dioxane* (EPA, 2015) and received public comments. As part of this scope, EPA developed an initial life cycle diagram and initial conceptual models for 1,4-dioxane that reconsidered all information under the amended law.

Historically, 90% of 1,4-dioxane production was used as a stabilizer in chlorinated solvents such as 1,1,1-trichloroethane (TCA). Use of 1,4-dioxane has decreased since TCA was phased out by the Montreal Protocol in 1996. 1,4-Dioxane is currently used in industrial processes and for industrial and commercial uses. Industrial processing uses include use as a processing aid and in functional fluids in closed systems. 1,4-Dioxane has uses as a laboratory chemical reagent, in adhesives and sealants and several other identified uses. Based on data from the 2016 Chemical Data Reporting (CDR), the current production volume is approximately 1 million pounds per year (U.S. EPA, 2016b). The most recent data on environmental releases, according to the Toxics Release Inventory (TRI), indicate that approximately 675,000 pounds of 1,4-dioxane were released to the environment in 2015 (U.S. EPA, 2017c). Releases are reported to all types of environmental media: air, water and land. The environmental fate of 1,4-dioxane is characterized by partitioning to the atmosphere, surface water and groundwater, and degradation by atmospheric oxidation or biodegradation. It is expected to be moderately persistent in the environment and have a low bioaccumulation potential.

The initial conceptual models presented in Section 2 identify conditions of use; exposure pathways (e.g., media); exposure routes (e.g., inhalation, dermal, oral); potentially exposed populations, including potentially exposed or susceptible subpopulations; and hazards EPA expects to evaluate based on the inherent hazards of the chemical.

This document presents the occupational scenarios in which workers and occupational non-users may be exposed to 1,4-dioxane during conditions of use, such as manufacturing, processing, repackaging and recycling. For 1,4-dioxane, EPA believes that workers and bystanders as well as certain other groups of individuals may experience greater exposures than the general population. EPA will evaluate whether other groups of individuals within the general population may be exposed via pathways that are distinct from the general population due to unique characteristics (e.g., life stage, behaviors, activities, duration) or have greater susceptibility than the general population, and should therefore be considered relevant potentially exposed or susceptible subpopulations for purposes of this risk evaluation.

Exposures to workers and/or the general population may occur from industrial releases and industrial and commercial uses. Environmental releases of 1,4-dioxane are reported in the Toxics Release Inventory to air, water or land. 1,4-Dioxane is stable under environmental conditions and does not degrade or react to any appreciable extent in the environment.

1,4-Dioxane has been the subject of several health hazard and risk assessments, based on data in animal studies. Any existing assessments will be a starting point as EPA will conduct a systematic review of the literature, including new literature since the existing assessments, as available in *1,4-*

*Dioxane (CASRN 123-91-1) Bibliography: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0723). EPA expects to consider human health hazards of 1,4-dioxane including acute toxicity, non-cancer effects and cancer. Non-cancer effects include irritation of the eyes and respiratory tract, liver toxicity and kidney toxicity. Animals exposed to 1,4-dioxane by inhalation and oral exposure have developed multiple types of cancer.

The initial analysis plan describes EPA's plan for conducting systematic review of readily available information and identification of assessment approaches to be used in conducting the risk evaluation for 1,4-dioxane. The initial analysis plan will be used to develop the problem formulation and final analysis plan for the risk evaluation of 1,4-dioxane.

# 1 INTRODUCTION

This document presents the scope of the risk evaluation to be conducted for 1,4-dioxane. If a condition of use has not been discussed, EPA, at this point in time, is not intending to include that condition of use in the scope of the risk evaluation. Moreover, during problem formulation EPA may determine that not all conditions of use mentioned in this scope will be included in the risk evaluation. Any condition of use that will not be evaluated will be clearly described in the problem formulation document.

On June 22, 2016, the Frank R. Lautenberg Chemical Safety for the 21st Century Act, which amended the Toxic Substances Control Act (TSCA), the Nation's primary chemicals management law, was signed into law. The new law includes statutory requirements and deadlines for actions related to conducting risk evaluations of existing chemicals.

TSCA § 6(b)(4) requires the United States Environmental Protection Agency (U.S. EPA) to establish a risk evaluation process. In performing risk evaluations for existing chemicals, EPA is directed to "determine whether a chemical substance presents an unreasonable risk of injury to health or the environment, without consideration of costs or other non-risk factors, including an unreasonable risk to a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation by the Administrator under the conditions of use."

In December of 2016, EPA published a list of 10 chemical substances that are the subject of the Agency's initial chemical risk evaluations (81 FR 91927), as required by TSCA § 6(b)(2)(A). These 10 chemical substances were drawn from the 2014 update of EPA's TSCA Work Plan for Chemical Assessments, a list of chemicals that EPA identified in 2012 and updated in 2014 (currently totaling 90 chemicals) for further assessment under TSCA. EPA's designation of the first 10 chemical substances constituted the initiation of the risk evaluation process for each of these chemical substances, pursuant to the requirements of TSCA § 6(b)(4).

TSCA § 6(b)(4)(D) requires that EPA publish the scope of the risk evaluation to be conducted, including the hazards, exposures, conditions of use and potentially exposed or susceptible subpopulations that the Administrator expects to consider. On February 14, 2017, EPA convened a public meeting to receive input and information to assist the Agency in its efforts to establish the scope of the risk evaluations under development for the ten chemical substances designated in December 2016 for risk evaluations pursuant to TSCA. EPA provided the public an opportunity to identify information, via oral comment or by submission to a public docket, specifically related to the conditions of use for the ten chemical substances. EPA used this information in developing this scope document, which fulfills the TSCA § 6(b)(4)(D) requirement for 1,4-dioxane.

As per the rulemaking, *Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act (TSCA)*, in conducting a risk evaluation under TSCA EPA will first identify "circumstances" that constitute "conditions of use" for each chemical. While EPA interprets this as largely a factual determination —i.e., EPA is to determine whether a chemical substance is actually involved in one or more of the activities listed in the definition—the determination will inevitably involve the exercise of some discretion. Based on legislative history, statutory structure and other evidence of Congressional intent, EPA has determined that certain activities may not generally be considered to be conditions of use. In exercising its discretion, for example, EPA would not generally consider that a single unsubstantiated or anecdotal statement (or even a few isolated statements) on the internet that a chemical can be used for a particular purpose would necessitate concluding that this represented part of the chemical substance's "conditions of use." As a further example, although the definition could be read literally to include all intentional misuses (e.g., inhalant abuse), as a "known" or "reasonably foreseen" activity in some circumstances, EPA does not generally intend to include such activities in either a chemical substance's prioritization or risk evaluation. In addition, EPA interprets the mandates under section 6(a)-(b) to conduct risk evaluations and any corresponding risk management to focus on uses for which manufacture, processing, or distribution in commerce is intended, known to be occurring, or reasonably foreseen (i.e., is prospective or on-going), rather than reaching back to evaluate the risks associated with legacy uses, associated disposal, and legacy disposal, and interprets the definition of "conditions of use" in that context. For instance, the conditions of use for purposes of section 6 might reasonably include the use of a chemical substance in insulation where the manufacture, processing or distribution in commerce for that use is prospective or on-going, but would not include the use of the chemical substance in currently installed insulation, if the manufacture, processing or distribution for that use is not prospective or on-going. In other words, EPA interprets the risk evaluation process of section 6 to focus on the continuing flow of chemical substances from manufacture, processing and distribution in commerce into the use and disposal stages of their lifecycle. That said, in a particular risk evaluation, EPA may consider background exposures from legacy use, associated disposal, and legacy disposal as part of an assessment of aggregate exposure or as a tool to evaluate the risk of exposures resulting from non-legacy uses.

Furthermore, in exercising its discretion under section 6(b)(4)(D) to identify the conditions of use that EPA expects to consider in a risk evaluation, EPA believes it is important for the Agency to have the discretion to make reasonable, technically sound scoping decisions in light of the overall objective of determining whether chemical substances in commerce present an unreasonable risk. Consequently, EPA may, on a case-by case basis, exclude certain activities that EPA has determined to be conditions of use in order to focus its analytical efforts on those exposures that are likely to present the greatest concern meriting an unreasonable risk consideration. For example, EPA intends to exercise discretion in addressing circumstances where the chemical substance subject to scoping is unintentionally present as an impurity in another chemical substance that is not the subject of the pertinent scoping, in order to determine which risk evaluation the potential risks from the chemical substance should be addressed in. As an additional example, EPA may, on a case-by-case basis, exclude uses that EPA has sufficient basis to conclude would present only "*de minimis*" exposures. This could include uses that occur in a closed system that effectively precludes exposure, or use as an intermediate. During the scoping phase, EPA may also exclude a condition of use that has been adequately assessed by another regulatory agency, particularly where the other agency has effectively managed the risks.

The situations identified above are examples of the kinds of discretion that EPA will exercise in determining what activities constitute conditions of use, and what conditions of use are to be included in the scope of any given risk evaluation. See the preamble to *Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act (TSCA)* for further discussion of these issues.

To the extent practicable, EPA has aligned this scope document with the approach set forth in the risk evaluation process rule; however, the scope documents for the first 10 chemicals in the risk evaluation process differ from the scope documents that EPA anticipates publishing in the future. The first

10 chemical substances were not subject to the prioritization process that will be used in the future in accordance with amendments to TSCA. EPA expects to collect and screen much of the relevant information about chemical substances that will be subject to the risk evaluation process during and before prioritization. The volume of data and information about the first 10 chemicals that is available to EPA is extremely large and EPA is still in the process of reviewing it, since the Agency had limited ability to process the information gathered before issuing the scope documents for the first 10 chemicals. As a result of the statutory timeframes, EPA had limited time to process all of the information gathered during scoping for the first 10 chemicals within the time provided in the statute for publication of the scopes after initiation of the risk evaluation process. For these reasons, EPA's initial screenings and designations with regard to applicability of data (e.g., on-topic vs. off-topic information and data) may change as EPA progresses through the risk evaluation process. Likewise, the Conceptual Models and Analysis Plans provided in the first 10 chemical scopes are designated as "Initial" to indicate that EPA expects to further refine them during problem formulation.

The aforementioned time constraints have resulted in scope documents for the first 10 chemicals that are not as refined or specific as future scope documents are anticipated to be. In addition, there was insufficient time for EPA to provide an opportunity for comment on a draft of this scope document, as it intends to do for future scope documents. For these reasons, EPA will publish and take public comment on a problem formulation document which will refine the current scope, as an additional interim step, prior to publication of the draft risk evaluations for the first 10 chemicals. This problem formulation is expected to be released within approximately 6 months of publication of the scope.

## 1.1 Regulatory History

EPA conducted a search of existing domestic and international laws, regulations and assessments pertaining to 1,4-dioxane. EPA compiled this summary from data available from federal, state, international and other government sources, as cited in Appendix A. EPA may evaluate and consider the impact of these existing laws and regulations in the problem formulation step to determine what, if any further analysis might be necessary as part of the risk evaluation.

***Federal Laws and Regulations***

1,4-Dioxane is subject to federal statutes or regulations, other than TSCA, that are implemented by other offices within EPA and/or other federal agencies/departments. A summary of federal laws, regulations and implementing authorities is provided in Appendix A.1.

***State Laws and Regulations***

1,4-Dioxane is subject to state statutes or regulations implemented by state agencies or departments. A summary of state laws, regulations and implementing authorities is provided in Appendix A.2.

***Laws and Regulations in Other Countries and International Treaties or Agreements***

1,4-Dioxane is subject to statutes or regulations in countries other than the United States and/or international treaties and/or agreements. A summary of these laws, regulations, treaties and/or agreements is provided in Appendix A.3.

## 1.2 Assessment History

EPA has identified assessments conducted by other EPA Programs and other organizations (see Table 1-1). Depending on the source, these assessments may include information on conditions of use, hazards, exposures and potentially exposed or susceptible subpopulations—information useful to EPA in preparing this scope for risk evaluation. Table 1-1 shows the assessments that have been conducted. In addition to using this information, EPA intends to conduct a full review of the data collected (see *1,4-Dioxane (CASRN 123-91-1) Bibliography: Supplemental File for the TSCA Scope Document*, EPA-HQ-OPPT-2016-0723) using the literature search strategy (see *Strategy for Conducting Literature Searches for 1,4-Dioxane: Supplemental File for the TSCA Scope Document*, EPA-HQ-OPPT-2016-0723) to ensure that EPA is considering information that has been made available since these assessments were conducted.

In 2015, EPA/OPPT published a Problem Formulation and Initial Assessment for 1,4-Dioxane (EPA, 2015) and received public comments. As part of this scope, EPA developed an initial life cycle diagram and initial conceptual models for 1,4-dioxane that re-considered all information under the amended law.

**Table 1-1. Assessment History of 1,4-Dioxane**

| Authoring Organization | Assessment |
|---|---|
| **EPA assessments** | |
| EPA, Office of Chemical Safety and Pollution Prevention (OCSPP), Office of Pollution Prevention and Toxics (OPPT) | TSCA Work Plan Chemical Problem Formulation and Initial Assessment: 1,4-Dioxane (CASRN 123-91-1) (2015b) |
| EPA, National Center for Environmental Assessment (NCEA) | Toxicological Review of 1,4-Dioxane (With Inhalation Update) (CASRN 123-91-1) (2013) |
| EPA, NCEA | Toxicological review of 1,4-Dioxane (CAS No. 123-91-1) (2010) |
| EPA, Office of Water (OW) | Drinking Water Health Advisory (U.S. EPA, 2012a) |
| **Other U.S.-based organizations** | |
| National Toxicology Program (NTP) | Report on Carcinogens, Fourteenth Edition, 1,4-Dioxane (2016) |
| Agency for Toxic Substances and Disease Registry (ATSDR) | Toxicological Profile for 1,4-Dioxane (2012) |
| National Advisory Committee for Acute Exposure Guideline Levels for Hazardous Substances (NAC/AEGL Committee) | Interim Acute Exposure Guideline Levels (AEGL) for 1,4-Dioxane (CAS Reg. No. 123-91-1) (2005b) |
| **International** | |
| International Cooperation on Cosmetics Regulation | Report of the ICCR Working Group: Considerations on Acceptable Trace Level of 1.4-Dioxane in Cosmetic Products (2017) |

| Authoring Organization | Assessment |
|---|---|
| International Agency for Research on Cancer (IARC) | IARC Monographs on the Evaluation of Carcinogenic Risks to Humans Volume 71 (1999) |
| Government of Canada, Environment Canada, Health Canada | Screening Assessment for the Challenge. 1,4-Dioxane. CASRN 123-91-1 (2010) |
| Research Center for Chemical Risk Management, National Institute of Advanced Industrial Science and Technology, Japan | Estimating Health Risk from Exposure to 1,4-Dioxane in Japan (2006) |
| World Health Organisation (WHO) | 1,4-Dioxane in Drinking-water (2005) |
| Employment, Social Affairs, and Inclusion, European Commission (EC) | Recommendation from the Scientific Committee on Occupational Exposure Limits for 1,4-dioxane (2004) |
| European Chemicals Bureau, Institute for Health and Consumer Protection | European Union Risk Assessment Report. 1,4-dioxane. CASRN 123-91-1. EINECS No: 204-661-8. (2002) |
| National Industrial Chemicals Notification and Assessment Scheme (NICNAS), Australian Government | 1,4-Dioxane. Priority Existing Chemical No. 7. Full Public Report (1998) |
| Organisation for Economic Co-operation and Development (OECD), Screening Information Data Set (SIDS) | 1,4-Dioxane. SIDS initial assessment profile (1999) |

## 1.3 Data and Information Collection

EPA/OPPT generally applies a process and workflow that includes: (1) data collection, (2) data evaluation and (3) data integration of the scientific data used in risk assessments developed under TSCA. Scientific analysis is often iterative in nature as new knowledge is obtained. Hence, EPA/OPPT expects that multiple refinements regarding data collection will occur during the process of risk evaluation.

***Data Collection: Data Search***

EPA/OPPT conducted chemical-specific searches for data and information on: physical and chemical properties; environmental fate and transport; conditions of use information; environmental exposures, human exposures, including potentially exposed or susceptible subpopulations; ecological hazard, human health hazard, including potentially exposed or susceptible subpopulations.

EPA/OPPT designed its initial data search to be broad enough to capture a comprehensive set of sources containing data and/or information potentially relevant to the risk evaluation. Generally, the search was not limited by date and was conducted on a wide range of data sources, including but not limited to: peer-reviewed literature and gray literature (e.g., publicly-available industry reports, trade association resources, government reports). When available, EPA/OPPT relied on the search strategies from recent assessments, such as EPA Integrated Risk Information System (IRIS) assessments and the NTP *Report on Carcinogens,* to identify relevant references and supplemented these searches to identify relevant information published after the end date of the previous search to capture more recent literature. *Strategy for Conducting Literature Searches for 1,4-Dioxane: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0723) provides details about the data sources and search terms that were used in the initial search.

***Data Collection: Data Screening***
Following the data search, references were screened and categorized using selection criteria outlined in the *Strategy for Conducting Literature Searches for 1,4-Dioxane: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0723). Titles and abstracts were screened against the criteria as a first step with the goal of identifying a smaller subset of the relevant data to move into the subsequent data extraction and data evaluation steps. Prior to full-text review, EPA/OPPT anticipates refinements to the search and screening strategies, as informed by an evaluation of the performance of the initial title/abstract screening and categorization process.

The categorization scheme (or tagging structure) used for data screening varies by scientific discipline (i.e., physical and chemical properties; environmental fate and transport; chemical use/conditions of use information; environmental exposures, human exposures, including potentially exposed or susceptible subpopulations identified by virtue of greater exposure; human health hazard, including potentially exposed or susceptible subpopulations identified by virtue of greater susceptibility; and ecological hazard), but within each data set, there are two broad categories or data tags: (1) o*n-topic* references or (2) *off-topic* references. *On-topic* references are those that may contain data and/or information relevant to the risk evaluation. O*ff-topic* references are those that do not appear to contain data or information relevant to the risk evaluation. The *Strategy for Conducting Literature Searches for 1,4-Dioxane: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0723) discusses the inclusion and exclusion criteria that EPA/OPPT used to categorize references as *on-topic* or *off-topic*.

Additional data screening using sub-categories (or sub-tags) was also performed to facilitate further sorting of data/information. For example, identifying references by source type (e.g., published peer-reviewed journal article, government report); data type (e.g., primary data, review article); human health hazard (e.g., liver toxicity, cancer, reproductive toxicity); or chemical-specific and use-specific data or information. These sub-categories are described in *Strategy for Conducting Literature Searches for 1,4-Dioxane: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0723) and will be used to organize the different streams of data during the stages of data evaluation and data integration steps of systematic review.

Results of the initial search and categorization results can be found in the *1,4-Dioxane (CASRN 123-91-1) Bibliography: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0723). This document provides a comprehensive list (bibliography) of the sources of data identified by the initial search and the initial categorization for *on-topic* and *off-topic* references. Because systematic review is an iterative process, EPA/OPPT expects that some references may move from the *on-topic* to the *off-topic* categories, and vice versa. Moreover, targeted supplemental searches may also be conducted to address specific needs for the analysis phase (e.g., to locate specific data needed for modeling); hence, additional *on-topic* references not initially identified in the initial search may be identified as the systematic review process proceeds.

# 2 SCOPE OF THE EVALUATION

As required by TSCA, the scope of the risk evaluation identifies the conditions of use, hazards, exposures and potentially exposed or susceptible subpopulations that the Administrator expects to consider. To communicate and visually convey the relationships between these components, EPA is including an initial life cycle diagram and initial conceptual models that describe the actual or potential relationships between 1,4-dioxane and human and ecological receptors. An initial analysis plan is also included which identifies, to the extent feasible, the approaches and methods that EPA may use to assess exposures, effects (hazards) and risks under the conditions of use of 1,4-dioxane. As noted previously, EPA intends to refine this analysis plan during the problem formulation phase of risk evaluation.

## 2.1 Physical and Chemical Properties

Physical-chemical properties influence the environmental behavior and the toxic properties of a chemical, thereby informing the potential conditions of use, exposure pathways and routes and hazards that EPA intends to consider. For scope development, EPA considered the measured or estimated physical-chemical properties set forth in Table 2-1.

**Table 2-1. Physical and Chemical Properties of 1,4-Dioxane**

| Property | Value [a] | References |
|---|---|---|
| Molecular formula | $C_4H_8O_2$ | |
| Molecular weight | 88.1 g/mole | Howard (1990) |
| Physical form | Clear liquid | (O'Neil et al., 2001) |
| Melting point | 11.75°C | (Haynes, 2014) |
| Boiling point | 101.1°C | O'Neil et al. (2006) |
| Density | 1.0329 g/cm$^3$ | (O'Neil et al., 2001) |
| Vapor pressure | 40 mm Hg at 25°C | Lewis (2000) |
| Vapor density | 3.03 (relative to air) | (Lewis, 2012) |
| Water solubility | >8.00 × 10$^2$ g/L | (Yalkowsky et al., 2010) |
| Octanol:water partition coefficient (log $K_{ow}$) | -0.27 | Hansch et al. (1995) |
| Henry's Law constant | 4.8 × 10$^{-6}$ atm-m$^3$/mole at 25°C<br>4.93 X 10$^{-4}$ atm-m$^3$/mole at 40°C | (Sander, 2017)<br>Howard (1990)<br>Atkins (1986) |
| Flash point | 18.3°C (open cup) | (Lewis, 2012) |
| Autoflammability | Not readily available | |
| Viscosity | 0.0120 cP at 25°C | (O'Neil, 2013) |
| Refractive index | 1.4224 at 20°C | (Haynes, 2014) |

| Property | Value [a] | References |
|---|---|---|
| Dielectric constant | 2.209 | Bruno and PDN (2006) |
| [a] Measured unless otherwise noted | | |

## 2.2 Conditions of Use

TSCA § 3(4) defines the conditions of use as "the circumstances, as determined by the Administrator, under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of."

### 2.2.1 Data and Information Sources

As the first step in preparing these scope documents, EPA identified, based on reasonably available information, the conditions of use for the subject chemicals. As further described in this document, EPA searched a number of available data sources (e.g. *Use and Market Profile for 1,4-Dioxane,* (EPA-HQ-OPPT-2016-0723). Based on this search, EPA published a preliminary list of information and sources related to chemical conditions of use (see *Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: 1,4-Dioxane*, EPA-HQ-OPPT-2017-0723-0003) prior to a February 2017 public meeting on scoping efforts for risk evaluation convened to solicit comment and input from the public. EPA also convened meetings with companies, industry groups, chemical users and other stakeholders to aid in identifying conditions of use and verifying conditions of use identified by EPA. The information and input received from the public and stakeholder meetings has been incorporated into this scope document to the extent appropriate, as indicated in Table 2-3. Thus, EPA believes the manufacture, processing, distribution, use and disposal activities identified in these documents constitute the intended, known, and reasonably foreseen activities associated with the subject chemicals, based on reasonably available information. The documents do not, in most cases, specify whether activity under discussion is intended, known, or reasonably foreseen, in part due to the time constraints in preparing these documents.

### 2.2.2 Identification of Conditions of Use

As part of the scope, an initial life cycle diagram is provided (Figure 2-1) depicting the conditions of use that are within the scope of the risk evaluation during various life cycle stages including manufacturing, processing, distribution, use (industrial, commercial, consumer; when distinguishable) and disposal. The information is grouped according to CDR processing codes and use categories (including functional use codes for industrial uses and product categories for industrial, commercial and consumer uses), in combination with other data sources (e.g., published literature and consultation with stakeholders) to provide an overview of conditions of use. EPA notes that some subcategories of use may be grouped under multiple CDR categories.

For the purposes of this scope, use categories include the following: "industrial use" means use at a site at which one or more chemicals or mixtures are manufactured (including imported) or processed. "Commercial use" means the use of a chemical or a mixture containing a chemical (including as part of an article) in a commercial enterprise providing saleable goods or services. "Consumer use" means the use of a chemical or a mixture containing a chemical (including as part of an article, such as furniture or clothing) when sold to or made available to consumers for their use (U.S. EPA, 2016b).

To understand conditions of use relative to one another and associated potential exposures under those conditions of use, the life cycle diagram includes the production volume associated with each stage of the life cycle, as reported in the 2016 CDR reporting (U.S. EPA, 2016b), when the volume was not claimed confidential business information (CBI). The 2016 CDR reporting data for 1,4-dioxane are provided in Table 2-2 for 1,4-dioxane from EPA's CDR database (U.S. EPA, 2016b).

**Table 2-2. Production Volume of 1,4-Dioxane in Chemical Data Reporting (CDR) Reporting Period (2012 to 2015) [a]**

| Reporting Year | 2012 | 2013 | 2014 | 2015 |
|---|---|---|---|---|
| Total Aggregate Production Volume (lbs) | 894,505 | 1,043,627 | 474,331 | 1,059,980 |

[a] The CDR data for the 2016 reporting period is available via ChemView (https://java.epa.gov/chemview) (U.S. EPA, 2016b). Because of an ongoing CBI substantiation process required by amended TSCA, the CDR data available in the scope document is more specific than currently in ChemView.

Figure 2-1 depicts the initial life cycle diagram of 1,4-dioxane from manufacture to the point of disposal. The total volume (in lbs) of 1,4-dioxane manufactured (including imported) in the U.S. from 2012 to 2015 indicates that production has varied over that time period. Historically, the main use (90%) of 1,4-dioxane was as a stabilizer of chlorinated solvents such as 1,1,1 trichloroethane (TCA) (ATSDR, 2012). Use of TCA was phased out under the 1995 Montreal Protocol and the use of 1,4-dioxane as a solvent stabilizer was terminated (NTP, 2016; ECJRC, 2002). Lack of recent reports for other previously reported uses (Sapphire Group, 2007) suggest that many other industrial, commercial and consumer uses were also stopped.

Descriptions of the industrial, commercial and consumer use categories identified from the 2016 CDR and included in the life cycle diagram are summarized below (U.S. EPA, 2016b). The descriptions provide a brief overview of the use category; Appendix B contains more detailed descriptions (e.g., process descriptions, worker activities, process flow diagrams, equipment illustrations) for each manufacture, processing, use and disposal category. The descriptions provided below are primarily based on the corresponding industrial function category and/or commercial and consumer product category descriptions from the 2016 CDR and can be found in EPA's Instructions for Reporting 2016 TSCA Chemical Data Reporting (U.S. EPA, 2016a).

As reflected in the initial life cycle diagram (Figure 2-1), intended, known and reasonably foreseen uses of 1,4-dioxane are primarily associated with industrial and commercial activities. Manufacturing sites produce 1,4-dioxane in liquid form at ≥90% concentration [EPA-HQ-OPPT-2016-0723-0012 (BASF, 2017)]. 1,4-Dioxane is currently used in industrial processes and for industrial and commercial uses. Industrial processing uses include use as a processing aid during wood pulping, pharmaceutical manufacture and etching of fluoropolymers and in functional fluids in closed systems. 1,4-Dioxane uses as a laboratory chemical reagent and in adhesives and sealants may occur in either industrial and/or commercial settings. A search for products containing 1,4-dioxane found several identified laboratory reference materials or standards containing 1,4-dioxane. In addition, two products with >5% of 1,4-dioxane: a professional film cement and a chemiluminescent laboratory reagent were identified. Other uses identified include use in fuels and fuel additives; spray polyurethane foam; and printing and printing compositions.

No consumer uses for 1,4-dioxane were reported in the U.S. in the 2016 CDR (U.S. EPA, 2016b). EPA did not identify any other U.S. sources that stated that 1,4-dioxane is currently used in the production of consumer products and, therefore, assumes that it is not. Other information sources do not differentiate between use of consumer and commercial products (ATSDR, 2012; U.S. EPA, 2006). A European risk assessment stated that 1,4-dioxane is used as a solvent in the production of several products that may be used by consumers like pharmaceuticals, pesticides, magnetic tape and adhesives (ECJRC, 2002). Public comments submitted by an industry coalition group (Public Comment, EPA-HQ-OPPT-2016-0723-0012) assert that 1,4-dioxane is not an intentionally added ingredient in any consumer products in the U.S.

1,4-Dioxane may be produced as a reaction by-product, particularly in chemicals which are produced by ethoxylation. These include alkyl ether sulphates (AES, anionic surfactants) and other ethoxylated substances, such as alkyl, alkylphenol and fatty amine ethoxylates; polyethylene glycols and their esters; and sorbitan ester ethoxylates. Therefore, 1,4-dioxane may be present at residual concentrations in commercial and consumer products that contain ethoxylated chemicals. Examples of products potentially containing 1,4-dioxane as a residual contaminant are paints, coatings, lacquers, ethylene glycol-based antifreeze coolants, spray polyurethane foam, household detergents, cosmetics/toiletries, textile dyes, pharmaceuticals, foods, agricultural and veterinary products (ATSDR, 2012; Health Canada, 2010; FDA, 2007; ECJRC, 2002). Manufacturers can apply controls to minimize the formation of 1,4-dioxane or remove most of the 1,4-dioxane present in these products through a vacuum stripping process (Public Comment, EPA-HQ-OPPT-2016-0723-0007) (ATSDR, 2012). The extent that manufacturers or processors apply controls or processes to minimize or remove 1,4-dioxane in surfactants during manufacture or before formulation in consumer products is unknown and likely varies by sector (ICCR, 2017).

1-4-Dioxane produced as a by-product of reactions in the production of other chemicals is excluded from the scope of the risk evaluation. EPA anticipates that 1,4-dioxane by-product and contaminant issues will be considered in the scope of any risk evaluation of ethoxylated chemicals.

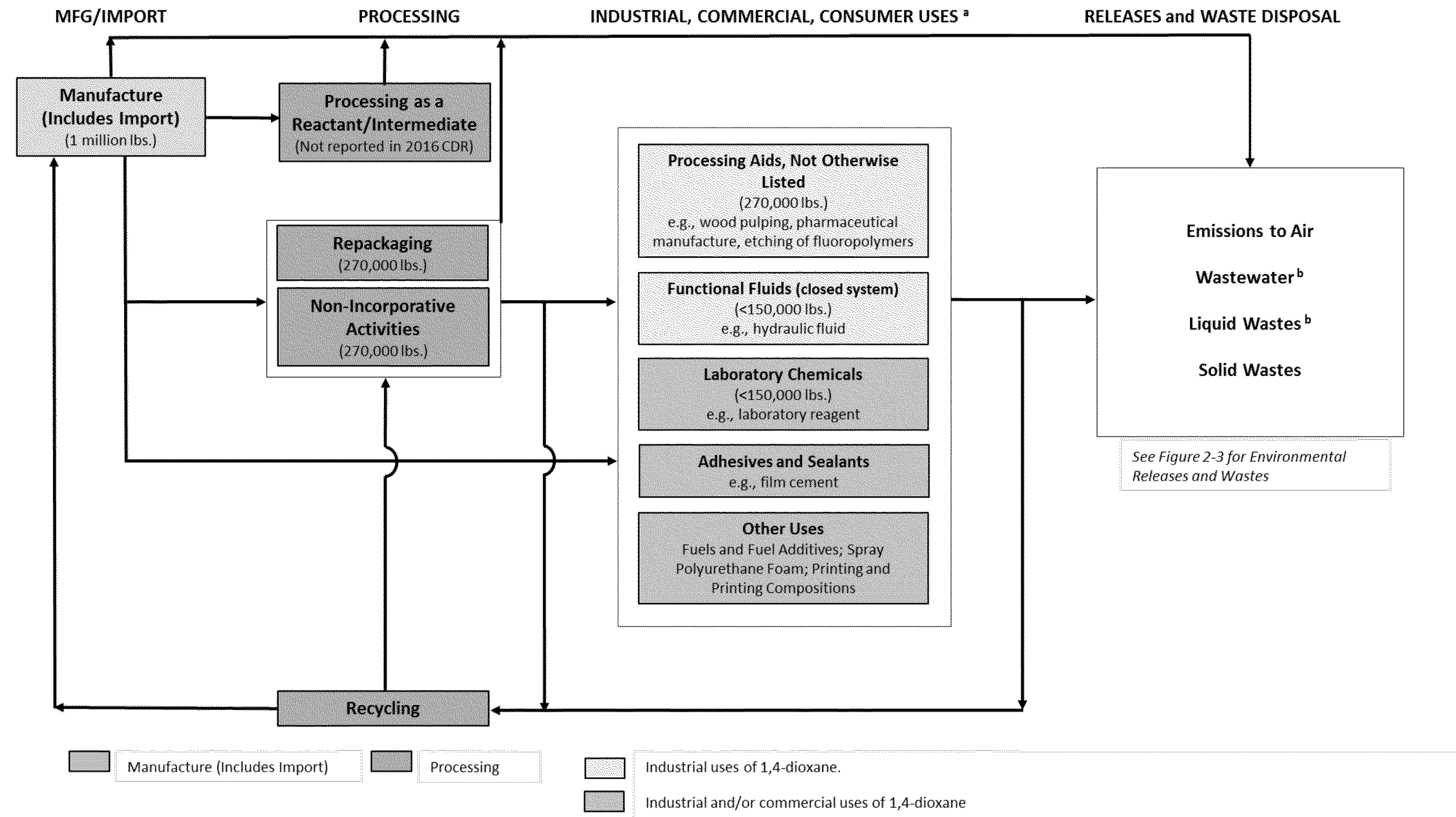



Figure 2-1. Initial 1,4-Dioxane Life Cycle Diagram

The initial life cycle diagram depicts the conditions of use that are within the scope of the risk evaluation during various life cycle stages including manufacturing, processing, use (industrial or commercial) and disposal. The production volumes shown are for reporting year 2015 from the 2016 CDR reporting period (U.S. EPA, 2016b). Activities related to distribution (e.g., loading, unloading) will be considered throughout the 1,4-dioxane life cycle, rather than using a single distribution scenario.

[a] See Table 2-3 for additional uses not mentioned specifically in this diagram.

[b] Wastewater: combination of water and organic liquid, where the organic content is <50%. Liquid Wastes: combination of water and organic liquid, where the organic content is >50%.

Table 2-3 summarizes each life cycle stage and the corresponding categories and subcategories of conditions of use for 1,4-dioxane that EPA expects to consider in the risk evaluation. Using the 2016 CDR, EPA identified industrial processing or use activities, industrial function categories and commercial use product categories. EPA identified the subcategories by supplementing CDR data with other published literature and information obtained through stakeholder consultations. For risk evaluations, EPA intends to consider each life cycle stage (and corresponding use categories and subcategories) and assess relevant potential sources of release and human exposure associated with that life cycle stage.

**Table 2-3. Categories and Subcategories of Conditions of Use of 1,4-Dioxane**

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| Manufacture | Domestic manufacture | Domestic manufacture | Use document, EPA-HQ-OPPT-2016-0723-0003; Public Comment, EPA-HQ-OPPT-2016-0723-0012 |
| | Import | Import | Use document, EPA-HQ-OPPT-2016-0723-0003 |
| Processing | Processing as a reactant | Pharmaceutical intermediate | Use document, EPA-HQ-OPPT-2016-0723-0003 |
| | | Polymerization catalyst | Use document, EPA-HQ-OPPT-2016-0723-0003 |
| | Non-incorporative | Pharmaceutical and medicine manufacturing (process solvent) | Public Comment, EPA-HQ-OPPT-2016-0723-0012 |
| | | Basic organic chemical manufacturing (process solvent) | Public Comment, EPA-HQ-OPPT-2016-0723-0012 |
| | Repackaging | Bulk to packages, then distribute | Public Comment, EPA-HQ-OPPT-2016-0723-0012 |
| | Recycling | Recycling | U.S. EPA (2017c) |
| Distribution in commerce | Distribution | Distribution in commerce | |
| Industrial use | Intermediate use | Agricultural chemical intermediate | Use document, EPA-HQ-OPPT-2016-0723-0003 |

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| | | Plasticizer intermediate | Use document, EPA-HQ-OPPT-2016-0723-0003 |
| | | Catalysts and reagents for anhydrous acid reactions, brominations and sulfonations | Use document, EPA-HQ-OPPT-2016-0723-0003 |
| | Processing aids, not otherwise listed | Wood pulping | Use document, EPA-HQ-OPPT-2016-0723-0003 |
| | | Extraction of animal and vegetable oils | Use document, EPA-HQ-OPPT-2016-0723-0003 |
| | | Wetting and dispersing agent in textile processing | Use document, EPA-HQ-OPPT-2016-0723-0003 |
| | | Polymerization catalyst | Use document, EPA-HQ-OPPT-2016-0723-0003 |
| | | Purification of pharmaceuticals | Use document, EPA-HQ-OPPT-2016-0723-0003 |
| | | Etching of fluoropolymers | Public Comment, EPA-HQ-OPPT-2016-0723-0012 |
| | Functional fluids (closed system) | Polyalkylene glycol lubricant | Use document, EPA-HQ-OPPT-2016-0723-0003 |
| | | Synthetic metalworking fluid | Use document, EPA-HQ-OPPT-2016-0723-0003 |
| | | Cutting and tapping fluid | Use document, EPA-HQ-OPPT-2016-0723-0003 |
| | | Hydraulic fluid | Use document, EPA-HQ-OPPT-2016-0723-0003 |
| Industrial use, potential commercial use | Laboratory chemicals | Chemical reagent | Use document, EPA-HQ-OPPT-2016-0723-0003; Public Comment, EPA-HQ-OPPT-2016-0723-0009 |

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| | | Reference material | Use document, EPA-HQ-OPPT-2016-0723-0003 |
| | | Spectroscopic and photometric measurement | Use document, EPA-HQ-OPPT-2016-0723-0003; Public Comment, EPA-HQ-OPPT-2016-0723-0009 |
| | | Liquid scintillation counting medium | Use document, EPA-HQ-OPPT-2016-0723-0003 |
| | | Stable reaction medium | Use document, EPA-HQ-OPPT-2016-0723-0003 |
| | | Cryoscopic solvent for molecular mass determinations | Use document, EPA-HQ-OPPT-2016-0723-0003 |
| | | Preparation of histological sections for microscopic examination | Use document, EPA-HQ-OPPT-2016-0723-0003 |
| | Adhesives and sealants | Film cement | Use document, EPA-HQ-OPPT-2016-0723-0003; Public Comment, EPA-HQ-OPPT-2016-0723-0021 |
| | Other uses | Fuels and fuel additives<br>Spray polyurethane foam<br>Printing and printing compositions | Use document, EPA-HQ-OPPT-2016-0723-0003; Public Comment, EPA-HQ-OPPT-2016-0723-0012 |
| Disposal | Emissions to air | Air | U.S. EPA (2017c) |
| | Wastewater | Industrial pre-treatment | |
| | | Industrial wastewater treatment | |
| | | Publicly owned treatment works (POTW) | |
| | | Underground injection | |
| | Solid wastes and liquid wastes | Municipal landfill | |
| | | Hazardous landfill | |

| Life Cycle Stage | Category [a] | Subcategory [b] | References |
|---|---|---|---|
| | | Other land disposal | |
| | | Municipal waste incinerator | |
| | | Hazardous waste incinerator | |
| | | Off-site waste transfer | |

[a] These categories of conditions of use appear in the initial life cycle diagram (Figure 2-1), reflect CDR codes and broadly represent conditions of use of 1,4-dioxane in industrial and/or commercial settings.
[b] These subcategories reflect more specific uses of 1,4-dioxane.

## 2.3 Exposures

For TSCA exposure assessments, EPA expects to evaluate exposures and releases to the environment resulting from the conditions of use applicable to 1,4-dioxane. Post-release pathways and routes will be described to characterize the relationship or connection between the conditions of use of 1,4-dioxane and the exposure to human receptors, including potentially exposed or susceptible subpopulations, and ecological receptors. EPA will take into account, where relevant, the duration, intensity (concentration), frequency and number of exposures in characterizing exposures to 1,4-dioxane.

### 2.3.1 Fate and Transport

Environmental fate includes both transport and transformation processes. Environmental transport is the movement of the chemical within and between environmental media. Transformation occurs through the degradation or reaction of the chemical with other species in the environment. Hence, knowledge of the environmental fate of the chemical informs the determination of the specific exposure pathways and potential human and environmental receptors EPA expects to consider in the risk evaluation. Table 2-4 provides environmental fate data that EPA has identified and considered in developing the scope for 1,4-dioxane.

**Table 2-4. Environmental Fate Characteristics of 1,4-Dioxane**

| Property or Endpoint | Value [a] | References |
|---|---|---|
| Direct photodegradation | Not expected to undergo direct photolysis | U.S. EPA (2015b) |
| Indirect photodegradation | 4.6 hours (estimated for atmospheric degradation) | U.S. EPA (2015b) |
| Hydrolysis half-life | Does not undergo hydrolysis | U.S. EPA (2015b) |
| Biodegradation | <10% in 29 days (aerobic in water, OECD 301F)<br><5% in 60 days (aerobic in water, OECD 310)<br>0% in 120 days, 60% in 300 days (aerobic in soil microcosm) | U.S. EPA (2015b) |
| Bioconcentration factor (BCF) | 0.2-0.7 (OECD 305C) | U.S. EPA (2015b) |

| Property or Endpoint | Value [a] | References |
|---|---|---|
| Bioaccumulation factor (BAF) | 0.93 (estimated) | U.S. EPA (2012b) |
| Organic carbon:water partition coefficient (log $K_{oc}$) | 0.4 (estimated) | U.S. EPA (2015b) |
| [a] Measured unless otherwise noted. | | |

1,4-Dioxane is expected to volatilize from dry surfaces and dry soil due to its vapor pressure of 40 mm Hg at 25°C (Table 2-1). It reacts with hydroxyl radicals (OH□) in the atmosphere with an estimated indirect photolysis half-life on the order of hours. 1,4-Dioxane is not expected to be susceptible to direct photolysis under environmental conditions since this compound lacks functional groups that absorb light at visible-ultraviolet (UV) light wavelengths.

Due to its water solubility (>800 g/L; Table 2-1) and Henry's Law constant ($4.8 \times 10^{-6}$ atm-$m^3$/mole at 25°C; Table 2-1), 1,4-dioxane is expected to be slightly volatile from water surfaces and moist soil. Once it enters the environment, 1,4-dioxane is expected to be mobile in soil based on its organic carbon partition coefficient (estimated log $K_{oc}$ = 0.4) and may therefore migrate to surface waters and groundwater. 1,4-Dioxane will not hydrolyze in water because it does not have functional hydrolyzable groups.

In experimental studies, 1,4-dioxane has been demonstrated to be not readily biodegradable and was subject to biodegradation after acclimation in a soil microcosm. Measured bioconcentration factors for 1,4-dioxane are 0.7 or below and the estimated bioaccumulation factor is 0.93. Therefore, 1,4-dioxane has low bioaccumulation potential.

### 2.3.2 Releases to the Environment

Releases to the environment from conditions of use (e.g., industrial and commercial processes, commercial or consumer uses resulting in down-the-drain releases) are one component of potential exposure and may be derived from reported data that are obtained through direct measurement, calculations based on empirical data and/or assumptions and models.

A source of information that EPA expects to consider in evaluating exposure are data reported under the Toxics Release Inventory (TRI) program. Under the Emergency Planning and Community Right-to-Know Act (EPCRA) Section 313 rule, 1,4-Dioxane is a TRI-reportable substance effective January 1, 1987.

Table 2-5 provides production-related waste managed data (also referred to as waste managed) for 1,4-dioxane reported by industrial facilities to the TRI program for 2015. Table 2-6 provides more detailed information on the quantities released to air or water or disposed of on land.

**Table 2-5. Summary of 1,4-Dioxane TRI Production-Related Waste Managed in 2015 (lbs)**

| Number of Facilities | Recycling | Energy Recovery | Treatment | Releases [a,b,c] | Total Production Related Waste |
|---|---|---|---|---|---|
| 49 | 4,292 | 1,591,064 | 1,923,623 | 705,691 | 4,224,670 |

Data source: 2015 TRI Data (updated March 2017) U.S. EPA (2017c).
[a] Terminology used in these columns may not match the more detailed data element names used in the TRI public data and analysis access points.
[b] Does not include releases due to one-time event not associated with production such as remedial actions or earthquakes.
[c] Counts all releases including release quantities transferred and release quantities disposed of by a receiving facility reporting to TRI.

Facilities are required to report if they manufacture (including import) or process more than 25,000 pounds of 1,4-dioxane, or if they otherwise use more than 10,000 pounds of 1,4-dioxane. In 2015, 49 facilities reported a total of 4.2 million pounds of 1,4-dioxane waste managed. Of this total, over 4 thousand pounds were recycled, 1.6 million pounds were recovered for energy, 1.9 million pounds were treated and 700 thousand pounds were released to the environment.

Of the almost 700 thousand pounds of total releases, there were both stack and fugitive air releases, water releases, Class I underground injection, release to Resource Conservation and Recovery Act (RCRA) Subtitle C landfills and other land disposal (Table 2-6).

**Table 2-6. Summary of 1,4-Dioxane TRI Releases to the Environment in 2015 (lbs)**

| | Number of Facilities | Air Releases | | Water Releases | Land Releases | | | Other Releases [a] | Total Releases [b,c] |
|---|---|---|---|---|---|---|---|---|---|
| | | Stack Air Releases | Fugitive Air Releases | | Class I Under-ground Injection | RCRA Subtitle C Landfills | All other Land Disposal [a] | | |
| Subtotal | | 46,219 | 16,377 | | 563,976 | 13,376 | 49 | | |
| Totals | 49 | 62,596 | | 35,402 | 577,400 | | | 0 | 675,399 |

Data source: 2015 TRI Data (updated March 2017) U.S. EPA (2017c).
[a] Terminology used in these columns may not match the more detailed data element names used in the TRI public data and analysis access points.
[b] These release quantities include releases due to one-time events not associated with production such as remedial actions or earthquakes.
[c] Counts release quantities once at final disposition, accounting for transfers to other TRI reporting facilities that ultimately dispose of the chemical waste.

While production-related waste managed shown in Table 2-5 excludes any quantities reported as catastrophic or one-time releases (TRI section 8 data), release quantities shown in Table 2-6 include both production-related and non-routine quantities (TRI section 5 and 6 data). As a result, release quantities may differ slightly and may further reflect differences in TRI calculation methods for reported release range estimates (U.S. EPA, 2017c).

One source EPA will use to quantify releases of 1,4-dioxane is EPA's AP-42, *Compilation of Air Pollutant Emission Factors*. AP-42 section 6.13 on pharmaceuticals production provides general process and emissions information and the ultimate disposition of 1,4-dioxane (air, sewer, incineration, solid waste, product) by pharmaceutical manufacturers. Other sources of information provide evidence of releases of 1,4-dioxane, including National Emission Standards for Hazardous Air Pollutants (NESHAPs) promulgated under the Clean Air Act (CAA) or other EPA standards and regulations that set legal limits on the amount of 1,4-dioxane that can be emitted to a particular media. EPA expects to consider these and other available data in conducting the exposure assessment component of the risk evaluation for 1,4-dioxane.

### 2.3.3 Presence in the Environment and Biota

Monitoring studies or a collection of relevant and reliable monitoring studies provide(s) information that can be used in an exposure assessment. Monitoring studies that measure environmental concentrations or concentrations of chemical substances in biota provide evidence of exposure. Monitoring data were identified in EPA's data search for 1,4-dioxane.

Monitoring data (measured) from EPA's Air Quality System (AQS) and the open literature, as well as modeled estimates based on the National Air Toxics Assessment (NATA) and TRI emissions data suggest that 1,4-dioxane is present in ambient air. Monitored and modeled air concentrations from these sources suggest that many air concentrations may be low (i.e., <1 $\mu g/m^3$) and appear to have been higher in the past, possibly reflecting past uses (U.S. EPA, 2015a, 2011).

Indoor air monitoring data are available. One recent study reported annual average concentrations of 1,4-dioxane ranging from 0.01 to 0.11 $\mu g/m^3$ in several hundred homes in Germany (Wissenbach et al., 2016). Older indoor air monitoring studies are summarized in the U.S. EPA Voluntary Children's Chemical Evaluation Program (VCCEP) submission and report slightly higher concentrations, possibly reflecting past uses (Sapphire Group, 2007).

EPA's third Unregulated Contaminant Monitoring Rule (UCMR 3), published in 2012, required monitoring for 1,4-dioxane, along with 29 other contaminants. Over 28,000 drinking water samples were collected for chemicals suspected to be present in drinking water that lack health-based standards under the Safe Drinking Water Act.

Reported levels of 1,4-dioxane in groundwater range from 3 to 31,000 µg/L (ATSDR, 2012; USGS, 2002). Such instances of ground water contamination with 1,4-dioxane are documented in the states of California and Michigan. These data provide a basis for including groundwater in the scope of the 1,4-dioxane risk evaluation from manufacturing, processing, distribution and use unless otherwise regulated or managed.

There are relatively fewer data available on 1,4-dioxane levels in surface water, though some studies of groundwater contamination also reported levels in nearby surface water. 1,4-Dioxane is released into surface water and some studies have examined 1,4-dioxane levels in sewage treatment or chemical plant effluent, combined collection treatments from apartment homes, and in river basin systems (ATSDR, 2012). 1,4-Dioxane has also been detected in landfill leachate. These data are consistent with including releases to surface water within the scope of 1,4-dioxane.

1,4-Dioxane has not been measured and is unlikely to be present in sediment, sludge, soil or dust, based on its physical and chemical properties. 1,4-Dioxane has a low bioaccumulation potential for accumulation in aquatic organisms and is short-lived in humans and few biomonitoring data are available.

### 2.3.4 Environmental Exposures

The manufacturing, processing, use and disposal of 1,4-dioxane can result in releases to the environment. EPA expects to consider exposures to the environment and ecological receptors that occur via the exposure pathways or media shown in Figure 2-3 in conducting the risk evaluation for 1,4-dioxane.

### 2.3.5 Human Exposures

EPA expects to consider three broad categories of human exposures: occupational exposures, consumer exposures and general population exposures. Subpopulations within these exposure categories will also be considered as described herein.

#### 2.3.5.1 Occupational Exposures

EPA expects to consider worker activities where there is a potential for exposure under the various conditions of use described in Section 2.2. In addition, EPA expects to consider exposure to occupational non-users, who do not directly handle the chemical but perform work in an area where the chemical is present. When data and information are available to support the analysis, EPA also expects to consider the effect(s) that engineering controls and/or personal protective equipment have on occupational exposure levels.

Workers and occupational non-users may be exposed to 1,4-dioxane when performing activities associated with the conditions of use described in Section 2.2, including, but not limited to:

- Unloading and transferring 1,4-dioxane to and from storage containers to process vessels.
- Using 1,4-dioxane in process equipment.
- Cleaning and maintaining equipment.
- Sampling chemical, formulations or products containing 1,4-dioxane for quality control.
- Repackaging chemicals, formulations or products containing 1,4-dioxane.
- Handling, transporting and disposing waste containing 1,4-dioxane.
- Performing other work activities in or near areas where 1,4-dioxane is used.

Based on these activities, EPA expects to consider inhalation exposure to vapors and mists and dermal exposure, including skin contact with vapors, liquids and mists for workers and occupational non-users. EPA also expects to consider potential worker exposure through mists that deposit in the upper respiratory tract and are swallowed.

The United States has several regulatory and non-regulatory exposure limits for 1,4-dioxane: An Occupational Safety and Health Administration (OSHA) Permissible Exposure Limit (PEL) of 100 ppm 8-hour time-weighted average (TWA) (360 mg/m$^3$) with a skin notation, a National Institute of Occupational Safety and Health (NIOSH) Recommended Exposure Limit (REL) of 1 ppm (3.6 mg/m$^3$) as a 30-minute ceiling and an American Conference of Government Industrial Hygienists (ACGIH) Threshold Limit Value (TLV) of 20 ppm TWA (72 mg/m$^3$) (OSHA, 2005). The influence of these exposure limits on occupation exposures will be considered in the occupational exposure assessment.

Key data that inform occupational exposure assessment and which EPA expects to consider include: the OSHA Chemical Exposure Health Data (CEHD) and NIOSH Health Hazard Evaluation (HHE) program data. OSHA data are workplace monitoring data from OSHA inspections. The inspections can be random or targeted, or can be the result of a worker complaint. OSHA data can be obtained through the OSHA Integrated Management Information System (IMIS) at https://www.osha.gov/oshstats/index.html. Table_Apx B-1 in Appendix B.2 provides a summary of industry sectors with 1,4-dioxane personal monitoring air samples obtained from OSHA inspections conducted between 2002 and 2016. NIOSH HHEs are conducted at the request of employees, union officials, or employers and help inform potential hazards at the workplace. HHEs can be downloaded at https://www.cdc.gov/niosh/hhe/. During the problem formulation, EPA will review these data and evaluate their utility in the risk evaluation.

#### 2.3.5.2 Consumer Exposures

No consumer uses for 1,4-dioxane were reported to EPA (U.S. EPA, 2017a, 2016b). 1,4-Dioxane may be found as a contaminant in consumer products and/or commercial products that are readily available for public purchase. However, it is present as a result of by-product formation during manufacture of ethoxylated chemicals that are subsequently formulated into products.

EPA does not expect to consider exposures to consumers and bystanders from by-product or contaminant exposure in the risk evaluation for 1,4-dioxane. Rather, EPA anticipates that 1,4-dioxane by-product and contaminant issues will be considered in the scope of any risk evaluation of ethoxylated chemicals.

#### 2.3.5.3 General Population Exposures

Wastewater/liquid wastes, solid wastes or air emissions of 1,4-dioxane could result in potential pathways for oral, dermal or inhalation exposure to the general population. EPA expects to consider each media, route and pathway to estimate general population exposures.

***Inhalation***

There is inhalation exposure potential to 1,4-dioxane by breathing ambient air and indoor air. Ambient air exposures may occur from releases from industrial/commercial sources. Indoor air exposures may occur from infiltration from ambient air or emissions from tap water during activities such as showering and bathing. Based on the relatively high water solubility and relatively low Henry's law constant for 1,4-dioxane, 1,4-dioxane is only slightly volatile from water, though water temperature can also influence volatilization.

Based on these potential sources and pathways of exposure, EPA expects to consider inhalation exposures of the general population to 1,4-dioxane in air that may result from the conditions of use of 1,4-dioxane.

***Oral***

The general population may ingest 1,4-dioxane via contaminated drinking water. Based on reported uses, down-the-drain sources may contribute to surface water and drinking water levels. Therefore, there is potential oral exposure to 1,4-dioxane by ingestion of drinking water from surface water and ground water sources.

Based on these potential sources and pathways of exposure, EPA expects to consider oral exposures to the general population that may result from the conditions of use of 1,4-dioxane.

***Dermal***

Dermal exposure via water could occur through contact, such as washing and bathing, with tap water containing 1,4-dioxane. The source of the contaminated water could either be contaminated surface or ground waters.

Based on these potential sources and pathways of exposure, EPA expects to consider dermal exposures to the general population that may result from the conditions of use of 1,4-dioxane.

#### 2.3.5.4 Potentially Exposed or Susceptible Subpopulations

TSCA requires that the determination of whether a chemical substance presents an unreasonable risk include consideration of unreasonable risk to "a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation" by EPA. TSCA § 3(12) states that "the term 'potentially exposed or susceptible subpopulation' means a group of individuals within the general population identified by the Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, or the elderly."

In this section, EPA addresses the potentially exposed or susceptible subpopulations identified as relevant based on greater exposure. EPA will address the subpopulations identified as relevant based on greater susceptibility in the hazard section.

Of the human receptors identified in the previous sections, EPA identifies the following as potentially exposed or susceptible subpopulations due to their *greater exposure* that EPA expects to consider in the risk evaluation:

- Workers and occupational non-users.
- Other groups of individuals within the general population who may experience greater exposures due to their proximity to conditions of use identified in Section 2.2 that result in releases to the environment and subsequent exposures (e.g., individuals who live or work near manufacturing, processing, distribution, use or disposal sites).

In developing exposure scenarios, EPA will evaluate available data to ascertain whether some human receptor groups may be exposed via exposure pathways that may be distinct to a particular subpopulation or lifestage (e.g., children's crawling, mouthing or hand-to-mouth behaviors) and whether some human receptor groups may have higher exposure via identified pathways of exposure due to unique characteristics (e.g., activities, duration or location of exposure) when compared with the general population (U.S. EPA, 2006).

In summary, in the risk evaluation for 1,4-dioxane, EPA expects to consider the following potentially exposed groups of human receptors: workers and occupational non-users. As described above, EPA may also identify additional potentially exposed or susceptible subpopulations that will be considered based on greater exposure.

## 2.4 Hazards (Effects)

For scoping, EPA conducted comprehensive searches for data on hazards of 1,4-dioxane, as described in *Strategy for Conducting Literature Searches for 1,4-Dioxane: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0723). Based on initial screening, EPA expects to consider the hazards of 1,4-dioxane identified in this scope document. However, when conducting the risk evaluation, the relevance of each hazard within the context of a specific exposure scenario will be judged for appropriateness. For example, hazards that occur only as a result of chronic exposures may not be applicable for acute exposure scenarios. This means that it is unlikely that every hazard identified in the scope will be considered for every exposure scenario.

### 2.4.1 Environmental Hazards

For scoping purposes, EPA consulted the following sources of environmental hazard data for 1,4-dioxane: Health Canada (2010); OECD (1999); ECJRC (2002); NICNAS (1998). However, EPA also expects to consider other studies (e.g., more recently published, alternative test data) that have been published since these reviews, as identified in the literature search conducted by the Agency for 1,4-dioxane [*1,4-Dioxane (CASRN 123-91-1) Bibliography: Supplemental File for the TSCA Scope Document*, EPA-HQ-OPPT-2016-0723]. The OECD's High Production Volume (HPV) Chemicals program assessed environmental hazards from 1,4-dioxane to fish, aquatic invertebrates and aquatic plants exposed under acute and chronic exposure conditions. Exposure to 1,4-dioxane indicated acute toxicity to aquatic invertebrates, based on mortality and immobilization, chronic toxicity to aquatic invertebrates (growth and reproduction) and toxicity to aquatic plants (growth rate). No chronic effects occurred in fish exposed to 1,4-dioxane.

EPA expects to consider the hazards of 1,4-dioxane to aquatic organisms including fish, aquatic invertebrates and algae exposed to relevant media under acute and chronic exposure conditions. EPA does not expect to consider the hazards of 1,4-dioxane to sediment invertebrates and terrestrial organisms including soil invertebrates, birds and mammals because the physical and chemical properties and high mobility in soil make presence in these media unlikely (see Section 2.3.1).

### 2.4.2 Human Health Hazards

1,4-Dioxane has an existing EPA IRIS Assessment (U.S. EPA, 2013, 2010), ATSDR Toxicological Profile (ATSDR, 2012), Canada Screening Assessment (Health Canada, 2010), European Union (EU) Risk Assessment Report (ECJRC, 2002) and Interim AEGL (U.S. EPA, 2005b); hence, many of the hazards of 1,4-dioxane have been previously compiled and reviewed. EPA has relied heavily on these comprehensive reviews in preparing this scope. EPA also expects to consider other studies (e.g., more recently published, alternative test data) that have been published since these reviews, as identified in the literature search conducted by the Agency for 1,4-dioxane [*1,4-Dioxane* (*CASRN 123-91-1*) *Bibliography: Supplemental File for the TSCA Scope Document*, EPA-HQ-OPPT-2016-0723]. EPA expects to consider all potential hazards associated with 1,4-dioxane. Based on reasonably available information, the following are the hazards that have been identified in previous government documents and that EPA currently expects will likely be the focus of its analysis.

#### 2.4.2.1 Non-Cancer Hazards

***Acute Toxicity***

Effects following acute exposures were evaluated (U.S. EPA, 2005b). The Interim AEGLs (U.S. EPA, 2005b) evaluated acute toxicity and irritation and concluded that, in animals, acute toxic effects of 1,4-

dioxane include central nervous system depression, kidney and liver damage and irritation. Humans acutely exposed to 1,4-dioxane experienced irritation of the eyes, nose and throat, nausea and vomiting, coma and death. Also, 1,4-dioxane can cause narcosis in animals inhaling very high concentrations (U.S. EPA, 2005b).

***Irritation***

Acute inhalation studies in human volunteers noted irritation of the eyes, nose and throat (U.S. EPA, 2005b). In rats, 2 years of inhalation exposure to 1,4-dioxane, resulted in metaplasia, hyperplasia, atrophy, hydropic change, vacuolic change and preneoplastic cell proliferation in the nasal cavity (U.S. EPA, 2013).

***Liver Toxicity***

In subchronic and chronic repeated exposure studies conducted in rats and mice by the oral (via drinking water) and inhalation routes, evidence shows that 1,4-dioxane is toxic to the liver (U.S. EPA, 2013). Chronic administration of 1,4-dioxane via the drinking water resulted in hepatocellular degeneration and preneoplastic changes. Inhalation exposure to 1,4-dioxane resulted in necrosis of the centrilobular region and preneoplastic changes in the liver.

***Kidney Toxicity***

In subchronic and chronic repeated exposure studies conducted in rats and mice by the oral (via drinking water) and inhalation routes, evidence shows that 1,4-dioxane is toxic to the kidney (U.S. EPA, 2013). Kidney damage following drinking water exposure to 1,4-dioxane includes degeneration of cortical tubule cells, necrosis with hemorrhage and glomerulonephritis.

#### 2.4.2.2 Genotoxicity and Cancer Hazards

U.S. EPA (2013) concluded that overall, the available literature indicates that 1,4-dioxane is nongenotoxic or weakly genotoxic. Per EPA's Cancer Guidelines (U.S. EPA, 2005a), EPA concluded that "there is insufficient biological support for potential key events and to have reasonable confidence in the sequence of events and how they relate to the development of nasal tumors following exposure to 1,4-dioxane". The mode of action by which 1,4-dioxane produces liver, nasal, peritoneal (mesotheliomas) and mammary gland tumors was not conclusive, and the available data did not support any hypothesized carcinogenic mode of action for 1,4-dioxane.

EPA evaluated the weight of the evidence for cancer in humans and animals and concluded that 1,4-dioxane is "likely to be carcinogenic to humans" based on evidence of carcinogenicity in several 2-year bioassays (oral and inhalation) conducted in four strains of rats, two strains of mice and in guinea pigs (U.S. EPA, 2013). Human occupational studies into the association between 1,4-dioxane exposure and increased cancer risk are inconclusive because they are limited by small cohort size and a small number of reported cancer cases.

#### 2.4.2.3 Potentially Exposed or Susceptible Subpopulations

TSCA requires that the determination of whether a chemical substance presents an unreasonable risk include consideration of unreasonable risk to "a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation" by EPA. TSCA § 3(12) states that "the term 'potentially exposed or susceptible subpopulation' means a group of individuals within the general population identified by the Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, or the elderly." In developing the hazard assessments, EPA will evaluate available data to ascertain whether some human receptor groups may have greater susceptibility than the general population to the chemical's hazard(s).

The IRIS assessment for 1,4-dioxane U.S. EPA (2013) found no direct evidence that certain populations and lifestages may be more susceptible to 1,4-dioxane. Information on induction of liver enzymes, genetic polymorphisms and gender differences was inadequate to quantitatively assess toxicokinetic or toxicodynamic differences in 1,4-dioxane hazard between animals and humans and the potential variability in human susceptibility.

## 2.5 Initial Conceptual Models

A conceptual model describes the actual or predicted relationships between the chemical substance and receptors, either human or environmental. These conceptual models are integrated depictions of the conditions of use, exposures (pathways and routes), hazards and receptors. As part of the scope for 1,4-dioxane, EPA developed three conceptual models, presented here.

### 2.5.1 Initial Conceptual Model for Industrial and Commercial Activities and Uses: Potential Exposures and Hazards

Figure 2-2 presents the initial conceptual model for human receptors from industrial and commercial activities and uses of 1,4-dioxane. EPA expects that workers and occupational non-users may be exposed to 1,4-dioxane via dermal and inhalation routes during manufacturing, processing, distribution, use and disposal of 1,4-dioxane. EPA also expects to consider potential worker exposure through mists that deposit in the upper respiratory tract and are swallowed.

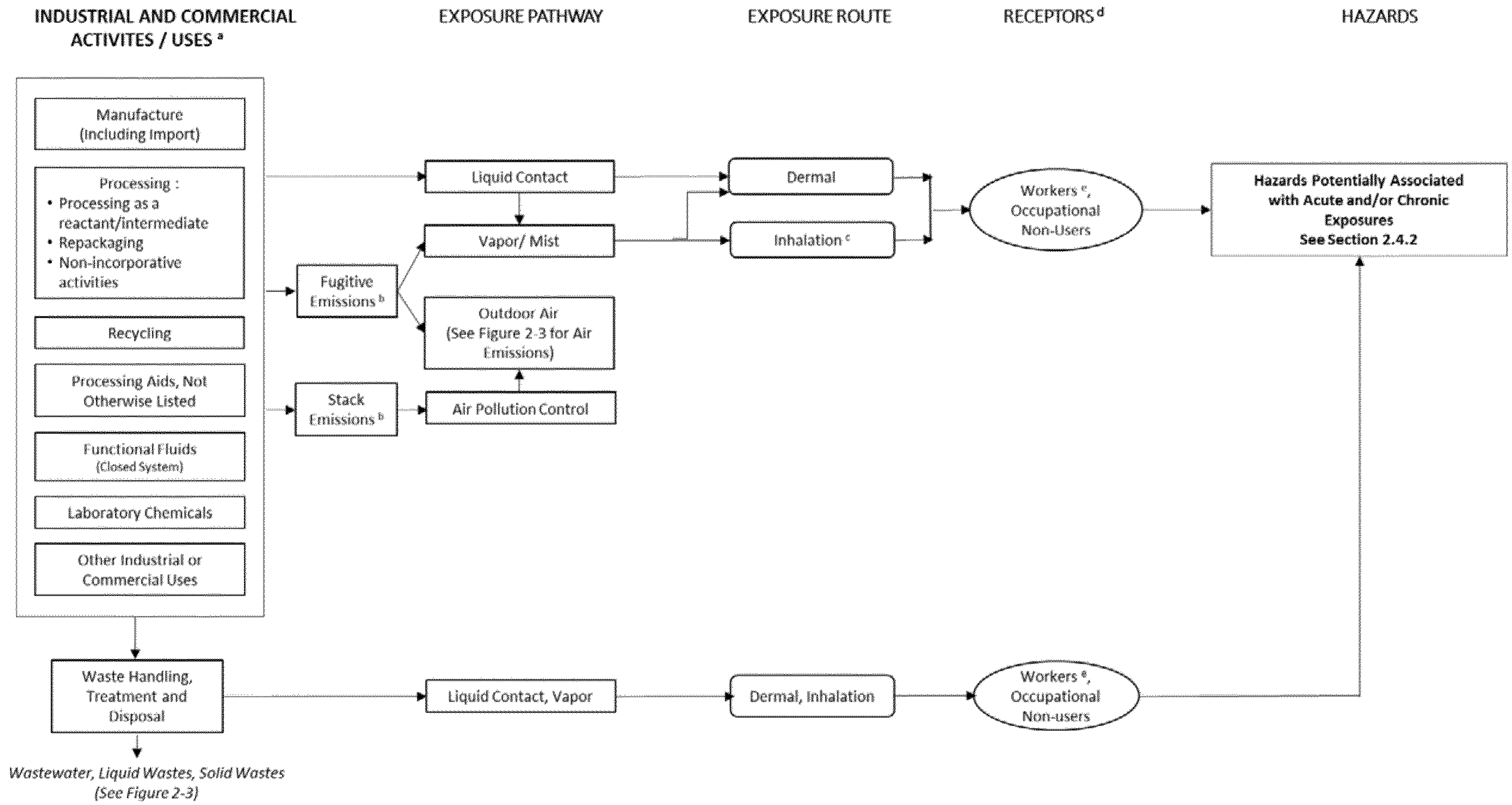



Figure 2-2. Initial 1,4-Dioxane Conceptual Model for Industrial and Commercial Activities and Uses: Potential Exposures and Hazards
The conceptual model presents the exposure pathways, exposure routes and hazards to human receptors from industrial and commercial activities and uses of 1,4-dioxane.

[a] Additional uses of 1,4-dioxane are included in Table 2-3.

[b] Stack air emissions are emissions that occur through stacks, confined vents, ducts, pipes or other confined air streams. Fugitive air emissions are those that are not stack emissions, and include fugitive equipment leaks from valves, pump seals, flanges, compressors, sampling connections, open-ended lines; evaporative losses from surface impoundment and spills; and releases from building ventilation systems.

[c] Exposure may occur through mists that deposit in the upper respiratory tract and are swallowed.

[d] Receptors include potentially exposed or susceptible subpopulations.

[e] When data and information are available to support the analysis, EPA also considers the effect that engineeringcontrols and/or personnel protective equipment have on occupational exposure levels.

### 2.5.2 Initial Conceptual Model for Consumer Activities and Uses: Potential Exposures and Hazards

As shown in the 1,4-dioxane initial life cycle diagram (Figure 2-1), no uses of 1,4-dioxane in consumer products have been identified.

### 2.5.3 Initial Conceptual Model for Environmental Releases and Wastes: Potential Exposures and Hazards

Figure 2-3 illustrates exposure pathways for human and ecological receptors from environmental releases and waste disposal activities.

As shown in Figure 2-3, the potential pathways from industrial and commercial activities and waste streams reflect the possible exposures to human and ecological receptors. EPA expects the general populations living near industrial and commercial facilities using 1,4-dioxane will be exposed via inhalation of outdoor air. General populations may also be exposed via ingestion of contaminated drinking water, dermal and inhalation exposure from showering/bathing with contaminated drinking water, and inhalation exposure from the migration of vapor in air, soil, or ground water to air. Aquatic and terrestrial life may be exposed to 1,4-dioxane via contaminated surface water.

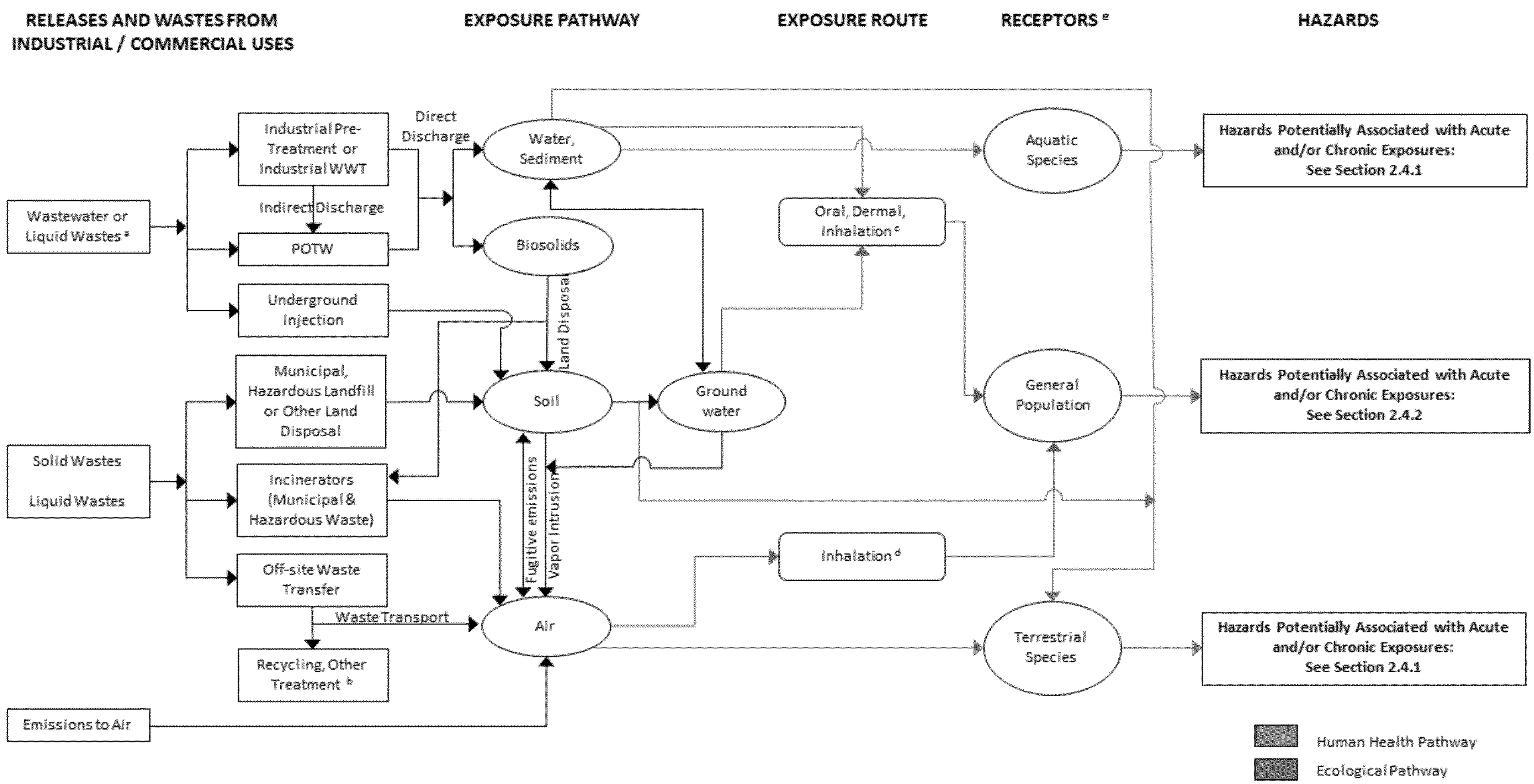



**Figure 2-3. Initial 1,4-Dioxane Conceptual Model for Environmental Releases and Wastes: Potential Exposures and Hazards**

The conceptual model presents the exposure pathways, exposure routes and hazards to human and environmental receptors from environmental releases and wastes of 1,4-dioxane.

[a] Industrial wastewater or liquid wastes may be treated on-site and then released to surface water (direct discharge), or pre-treated and released to POTW (indirect discharge). Drinking water will undergo further treatment in drinking water treatment plants. Ground water may also be a source of drinking water.

[b] Additional releases may occur from recycling and other waste treatment.

[d] Volatilization from or liquid contact with tap water in the home during showering, bathing, washing, etc. represents another potential in-home exposure pathway.

[e] Presence of mist is not expected; dermal and oral exposure are negligible.

[f] Receptors include potentially exposed or susceptible subpopulations.

## 2.6 Initial Analysis Plan

The initial analysis plan will be used to develop the eventual problem formulation and final analysis plan for the risk evaluation. While EPA has conducted a search for readily available data and information from public sources as described in Section 1.3, EPA encourages submission of additional existing data, such as full study reports or workplace monitoring from industry sources, that may be relevant for refining conditions of use, exposures, hazards and potentially exposed or susceptible subpopulations.

The analysis plan outlined here is based on the conditions of use of 1,4-dioxane, as described in Section 2.2 of this scope. The analysis plan may be refined as EPA proceeds with the systematic review of the information in the *1,4-Dioxane (CASRN 123-91-1) Bibliography: Supplemental File for the TSCA Scope Document* (EPA-HQ-OPPT-2016-0723*).* EPA will be evaluating the weight of the scientific evidence for both hazard and exposure. Consistent with this approach, EPA will also use a systematic review approach. As such, EPA will use explicit, pre-specified criteria and approaches to identify, select, assess, and summarize the findings of studies. This approach will help to ensure that the review is complete, unbiased, reproducible, and transparent.

### 2.6.1 Exposure

#### 2.6.1.1 Environmental Releases

EPA expects to consider and analyze releases to environmental media as follows:

1) Review reasonably available published literature or information on processes and activities associated with the conditions of use to evaluate the types of releases and wastes generated.
2) Review reasonably available chemical-specific release data, including measured or estimated release data (e.g., data collected under the TRI and National Emissions Inventory [NEI] programs).
3) Review reasonably available measured or estimated release data for surrogate chemicals that have similar uses, volatility, chemical and physical properties.
4) Understand and consider regulatory limits that may inform estimation of environmental releases.
5) Review and determine applicability of OECD Emission Scenario Documents and EPA Generic Scenarios to estimation of environmental releases.
6) Evaluate the weight of the evidence of environmental release data.
7) Map or group each condition(s) of use to a release assessment scenario.

#### 2.6.1.2 Environmental Fate

EPA expects to consider and analyze fate and transport in environmental media as follows:

1) Review reasonably available measured or estimated environmental fate endpoint data collected through the literature search.
2) Using measured data and/or modeling, determine the influence of environmental fate endpoints (e.g., persistence, bioaccumulation, partitioning, transport) on exposure pathways and routes of exposure to human and environmental receptors.
3) Evaluate the weight of the evidence of environmental fate data.

#### 2.6.1.3 Environmental Exposures

EPA expects to consider the following in developing its environmental exposure assessment of 1,4-dioxane:

1) Review reasonably available environmental and biological monitoring data for all media relevant to environmental exposure.
2) Review reasonably available information on releases to determine how modeled estimates of concentrations near industrial point sources compare with available monitoring data. Available exposure models will be evaluated and considered alongside available monitoring data to characterize environmental exposures. Modeling approaches to estimate surface water concentrations, sediment concentrations and soil concentrations generally consider the following inputs: release into the media of interest, fate and transport and characteristics of the environment.
3) Review reasonably available biomonitoring data. Consider whether these monitoring data could be used to compare with species or taxa-specific toxicological benchmarks.
4) Determine applicability of existing additional contextualizing information for any monitored data or modeled estimates during risk evaluation. Review and characterize the spatial and temporal variability, to extent data are available, and characterize exposed aquatic and terrestrial populations.
5) Evaluate the weight of evidence of environmental occurrence data and modeled estimates.
6) Map or group each condition(s) of use to environmental assessment scenario(s).

#### 2.6.1.4 Occupational Exposures

EPA expects to consider and analyze both worker and occupational non-user exposures as follows:

1) Review reasonably available exposure monitoring data for specific condition(s) of use. Exposure data to be reviewed may include workplace monitoring data collected by government agencies such as OSHA and the NIOSH, and monitoring data found in published literature (e.g., personal exposure monitoring data (direct measurements) and area monitoring data (indirect measurements).
2) Review reasonably available exposure data for surrogate chemicals that have uses, volatility and chemical and physical properties similar to 1,4-dioxane.
3) For conditions of use where data are limited or not available, review existing exposure models that may be applicable in estimating exposure levels.
4) Review reasonably available data that may be used in developing, adapting or applying exposure models to the particular risk evaluation.
5) Consider and incorporate applicable engineering controls and/or personal protective equipment into exposure scenarios.
6) Evaluate the weight of the evidence of occupational exposure data.
   Map or group each condition of use to occupational exposure assessment scenario(s).

#### 2.6.1.5 Consumer Exposures

EPA does not expect to consider and analyze consumer exposures in the risk evaluation (see Section 2.3.5.2).

#### 2.6.1.6 General Population

EPA expects to consider and analyze general population exposures as follows:

1) Review reasonably available environmental and biological monitoring data for media to which general population exposures are expected.
2) For exposure pathways where data are not available, review existing exposure models that may be applicable in estimating exposure levels.
3) Consider and incorporate applicable media-specific regulations into exposure scenarios or modeling.
4) Review reasonably available data that may be used in developing, adapting or applying exposure models to the particular risk evaluation. For example, existing models developed for a chemical assessment may be applicable to another chemical assessment if model parameter data are available.
5) Review reasonably available information on releases to determine how modeled estimates of concentrations near industrial point sources compare with available monitoring data.
6) Review reasonably available population- or subpopulation-specific exposure factors and activity patterns to determine if potentially exposed or susceptible subpopulations need be further defined.
7) Evaluate the weight of the evidence of general population exposure data.
8) Map or group each condition of use to general population exposure assessment scenario(s).

### 2.6.2 Hazards (Effects)

#### 2.6.2.1 Environmental Hazards

EPA expects to conduct an environmental hazard assessment of 1,4-dioxane as follows:

1) Review reasonably available environmental hazard data, including data from alternative test methods (e.g., computational toxicology and bioinformatics; high-throughput screening methods; data on categories and read-across; *in vitro* studies).
2) Conduct hazard identification (the qualitative process of identifying acute and chronic endpoints) and concentration-response assessment (the quantitative relationship between hazard and exposure) for all identified environmental hazard endpoints.
3) Derive concentrations of concern (COC) for all identified ecological endpoints.
4) Evaluate the weight of the evidence of environmental hazard data.
5) Consider the route(s) of exposure, available biomonitoring data and available approaches to integrate exposure and hazard assessments.

#### 2.6.2.2 Human Health Hazards

EPA expects to consider and analyze human health hazards as follows:

1) Review reasonably available human health hazard data, including data from alternative test methods (e.g., computational toxicology and bioinformatics; high-throughput screening methods; data on categories and read-across; *in vitro* studies; systems biology).
2) In evaluating reasonably available data, determine whether particular human receptor groups may have greater susceptibility to the chemical's hazard(s) than the general population.
3) Conduct hazard identification (the qualitative process of identifying non-cancer and cancer endpoints) and dose-response assessment (the quantitative relationship between hazard and exposure) for all identified human health hazard endpoints.

4) Derive points of departure (PODs) where appropriate; conduct benchmark dose modeling depending on the available data. Adjust the PODs as appropriate to conform (e.g., adjust for duration of exposure) to the specific exposure scenarios evaluated.
5) Evaluate the weight of the evidence of human health hazard data.
6) Consider the route(s) of exposure (oral, inhalation, dermal), available route-to-route extrapolation approaches, available biomonitoring data and available approaches to correlate internal and external exposures to integrate exposure and hazard assessment.

### 2.6.3 Risk Characterization

Risk characterization is an integral component of the risk assessment process for both ecological and human health risks. EPA will derive the risk characterization in accordance with EPA's *Risk Characterization Handbook* (U.S. EPA, 2000). As defined in EPA's *Risk Characterization Policy*, "the risk characterization integrates information from the preceding components of the risk evaluation and synthesizes an overall conclusion about risk that is complete, informative and useful for decision makers." Risk characterization is considered to be a conscious and deliberate process to bring all important considerations about risk, not only the likelihood of the risk but also the strengths and limitations of the assessment, and a description of how others have assessed the risk into an integrated picture.

Risk characterization at EPA assumes different levels of complexity depending on the nature of the risk assessment being characterized. The level of information contained in each risk characterization varies according to the type of assessment for which the characterization is written. Regardless of the level of complexity or information, the risk characterization for TSCA risk evaluations will be prepared in a manner that is transparent, clear, consistent and reasonable (TCCR) (U.S. EPA, 2000). EPA will also present information in this section consistent with approaches described in the Risk Evaluation Framework Rule.

# REFERENCES


Atkins, PW. (1986). Physical Chemistry. Oxford, England: Oxford University Press.

ATSDR (Agency for Toxic Substances and Disease Registry). (2012). Toxicological profile for 1,4 dioxane [ATSDR Tox Profile]. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. http://www.atsdr.cdc.gov/toxprofiles/tp.asp?id=955&tid=199

BASF. (2017). Information in Response to the "Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: 1,4-Dioxane" Document. https://www.regulations.gov/document?D=EPAHQ-OPPT-2016-0723-0012

Bruno, TJ; PDN, S. (2006). CRC Handbook of Fundamental Spectroscopic Correlation Charts. Boca Raton, FL: CRC Press. http://www.hbcpnetbase.com/

EC (European Commission). (2004). Recommendation from the Scientific Committee on Occupational Exposure Limits for 1,4-dioxane. Employment, Social Affairs and Inclusion. file:///C:/Users/26161/Saved%20Games/Downloads/SUM%20112%20new%20template%20WEB%20ready.pdf

ECJRC (European Commission, Joint Research Centre). (2002). European Union risk assessment report: 1,4-dioxane. (EUR 19833 EN). Luxembourg: Office for Official Publications of the European Communities. https://echa.europa.eu/documents/10162/a4e83a6a-c421-4243-a8df-3e84893082aa

FDA (U.S. Food and Drug Administration). (2007). 1,4-Dioxane- A Manufacturing Byproduct. Food and Drug Administration. http://www.fda.gov/cosmetics/productsingredients/potentialcontaminants/ucm101566.htm

Hansch, C; Leo, A; Hoekman, D. (1995). Exploring QSAR: Hydrophobic, electronic, and steric constants. In C Hansch; A Leo; DH Hoekman (Eds.), Exploring QSAR: Hydrophobic, Electronic, and Steric Constants. Washington, DC: American Chemical Society.

Haynes, WM. (2014). CRC handbook of chemistry and physics. In WM Haynes (Ed.), (95th ed.). Boca Raton, FL: CRC Press. https://www.crcpress.com/CRC -Handbook-of-Chemistry-and-Physics-95th-Edition/Haynes/p/book/9781482208689

Health Canada. (2010). Screening Assessment for the Challenge: 1,4-Dioxane. Environment Canada, Health Canada. http://www.ec.gc.ca/ese -ees/789BC96E-F970-44A7-B306-3E32419255A6/batch7_123-91-1_en.pdf

Howard, PH. (1990). Handbook of environmental fate and exposure data for organic chemicals: Volume II: Solvents. Syracuse, NY: CRC Press.

IARC (International Agency for Research on Cancer). (1999). IARC monographs on the evaluation of carcinogenic risks to humans: Re-evaluation of some organic chemicals, hydrazine and hydrogen peroxide [IARC Monograph]. Lyon, France: World Health Organization.

ICCR (International Cooperation on Cosmetics Regulation). (2017). Considerations on acceptable trace level of 1,4-dioxane in cosmetic products, final report. Report of the ICCR Working Group. http://www.iccrnet.org/files/2414/8717/1555/ICCR_14-Dioxane_Final_2017.pdf

Lewis, RJ, Sr. (2000). Sax's dangerous properties of industrial materials. In Sax's Dangerous Properties of Industrial Materials (10 ed.). New York, NY: John Wiley & Sons, Inc.

Lewis, RJ, Sr. (2012). Sax's dangerous properties of industrial materials. In RJ Lewis, Sr. (Ed.), (12th ed.). Hoboken, NJ: John Wiley & Sons, Inc. http://onlinelibrary.wiley.com/book/10.1002/0471701343

Makino, R; Kawasaki, H; Kishimoto, A; Gamo, M; Nakanishi, J. (2006). Estimating health risk from exposure to 1,4-dioxane in Japan. Environ Sci 13: 43-58.

NICNAS (National Industrial Chemicals Notification and Assessment Scheme). (1998). 1, 4-Dioxane. Priority existing chemical assessment report No. 7. Canberra, ACT: National Occupational Health and Safety Commission, Commonwealth of Australia. https://www.nicnas.gov.au/chemical-information/pec-assessments

NTP (National Toxicology Program). (2016). 14th Report On Carcinogens. Research Triangle Park, NC: U.S. Department of Health and Human Services, Public Health Service. https://ntp.niehs.nih.gov/pubhealth/roc/index1.html

O'Neil, MJ. (2013). The Merck index: An encyclopedia of chemicals, drugs, and biologicals. In MJ O'Neil (Ed.), (15th ed.). Cambridge, UK: Royal Society of Chemistry.

O'Neil, MJ; Heckelman, PE; Koch, CB. (2006). The Merck index: An encyclopedia of chemicals, drugs, and biologicals (14th ed.). Whitehouse Station, NJ: Merck & Co.

O'Neil, MJ; Smith, A; Heckelman, PE; Obenchain, JR; Gallipeau, JR; D'Arecca, MA. (2001). Dioxane. In MJ O'Neil; A Smith; PE Heckelman; JR Obenchain; JR Gallipeau; MA D'Arecca (Eds.), The Merck Index: An Encyclopedia of Chemicals, Drugs, and Biologicals (13th ed., pp. 3332). Whitehouse Station, NJ: Merck & Co., Inc.

OECD (Organisation for Economic Co-operation and Development). (1999). Screening information dataset (SIDS) initial assessment profile: 1,4 Dioxane. http://webnet.oecd.org/Hpv/UI/handler.axd?id=59ef0889-2583-4a94-ab54-00fcab06d81c

OECD (Organisation for Economic Co-operation and Development). (2015). Emission scenari0 document (ESD) on the use of adhesives. In Series on Emission Scenario Documents No 34. (ENV/JM/MONO(2015)4). Paris: ENVIRONMENT DIRECTORATE JOINT MEETING OF THE CHEMICALS COMMITTEE AND THE WORKING PARTY ON CHEMICALS, PESTICIDES AND BIOTECHNOLOGY. http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=ENV/JM/MONO(2015)4&doclanguage=en

OSHA (Occupational Safety & Health Administration). (2005). Chemical Sampling Information: Dioxane. Retrieved from https://www.osha.gov/dts/chemicalsampling/data/CH_237200.html

OSHA (Occupational Safety & Health Administration). (2017a). Chemical exposure health data (CEHD). Washington, DC: U.S. Department of Labor. Retrieved from https://www.osha.gov/opengov/healthsamples.html

OSHA (Occupational Safety & Health Administration). (2017b). Chemical Exposure Health Data (CEHD) provided by OSHA to EPA. U.S. Occupational Safety and Health Administration.

Sander, R. (2017). Henry's Law Constants in NIST chemistry WebBook: NIST standard reference database number 69. Available online at http://webbook.nist.gov/

Sapphire Group (Sapphire Group Inc.). (2007). Voluntary Children's Chemical Evaluation Program [VCCEP]. Tiers 1, 2, and 3 Pilot Submission For 1,4-Dioxane. Cleveland, OH: Sponsored by Ferro Corporation, Inc. http://www.tera.org/Peer/VCCEP/p- Dioxane/p-Dioxane%20Submission.pdf

U.S. EPA (U.S. Environmental Protection Agency). (2000). Science policy council handbook: Risk characterization (pp. 1-189). (EPA/100/B-00/002). Washington, D.C.: U.S. Environmental Protection Agency, Science Policy Council. https://www.epa.gov/risk/risk- characterization-handbook

U.S. EPA (U.S. Environmental Protection Agency). (2005a). Guidelines for carcinogen risk assessment [EPA Report] (pp. 1-166). (EPA/630/P-03/001F). Washington, DC: U.S. Environmental Protection

Agency, Risk Assessment Forum. http://www2.epa.gov/osa/guidelines -carcinogen-risk-assessment
U.S. EPA (U.S. Environmental Protection Agency). (2005b). Interim Acute Exposure Guideline Levels (AEGLs) 1,4-Dioxane. Washington, DC: NAS/COT Subcommittee for AEGLs. https://www.epa.gov/aegl/14 -dioxane-results-aegl-program
U.S. EPA (U.S. Environmental Protection Agency). (2006). A framework for assessing health risk of environmental exposures to children (pp. 1-145). (EPA/600/R-05/093F). Washington, DC: U.S. Environmental Protection Agency, Office of Research and Development, National Center for Environmental Assessment. http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=158363
U.S. EPA (U.S. Environmental Protection Agency). (2010). Toxicological review of 1,4-Dioxane (CAS No. 123-91-1) in support of summary information on the Integrated Risk Information System (IRIS) [EPA Report]. (EPA-635/R-09-005-F). Washington, DC. http://www.epa.gov/iris/toxreviews/0326tr.pdf
U.S. EPA (U.S. Environmental Protection Agency). (2011). Exposure factors handbook: 2011 edition (final). (EPA/600/R-090/052F). Washington, DC: U.S. Environmental Protection Agency, Office of Research and Development, National Center for Environmental Assessment. http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=236252
U.S. EPA (U.S. Environmental Protection Agency). (2012a). 2012 Edition of the drinking water standards and health adivsories. (EPA/822/S-12/001). Washington, DC: Office of Water. http://water.epa.gov/action/advisories/drinking/upload/dwstandards2012.pdf
U.S. EPA (U.S. Environmental Protection Agency). (2012b). Estimation Programs Interface (EPI) Suite™ for Microsoft® Windows (Version 4.11). Washington D.C.: Environmental Protection Agency. Retrieved from http://www.epa.gov/opptintr/exposure/pubs/episuite.htm
U.S. EPA (U.S. Environmental Protection Agency). (2013). Toxicological review of 1,4-Dioxane (with inhalation update) (CAS No. 123-91-1) in support of summary information on the Integrated Risk Information System (IRIS) [EPA Report]. (EPA-635/R-11/003-F). Washington, DC.
U.S. EPA (U.S. Environmental Protection Agency). (2015a). Air Quality System (AQS). Available online at http://www.epa.gov/aqs
U.S. EPA (U.S. Environmental Protection Agency). (2015b). TSCA Work Plan Chemical Problem Formulation and Initial Assessment. 1,4-Dioxane. (740-R1-5003). Washington, DC: Environmental Protection Agency, Office of Chemical Safety and Pollution Prevention. http://nepis.epa.gov/Exe/ZyPURL.cgi?Dockey=P100MDC1.TXT
U.S. EPA (U.S. Environmental Protection Agency). (2016a). Instructions for reporting 2016 TSCA chemical data reporting. https://www.epa.gov/chemical-data-reporting/instructions-reporting-2016-tsca-chemical-data-reporting
U.S. EPA (U.S. Environmental Protection Agency). (2016b). Public database 2016 chemical data reporting (May 2017 release). Washington, DC: US Environmental Protection Agency, Office of Pollution Prevention and Toxics. Retrieved from https://www.epa.gov/chemical-data-reporting
U.S. EPA (U.S. Environmental Protection Agency). (2017a). Internal communication. Washington, DC: U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics.
U.S. EPA (U.S. Environmental Protection Agency). (2017b). Preliminary information on manufacturing, processing, distribution, use, and disposal: 1,4 Dioxane. (EPA-HQ-OPPT-2016-0723). Office of Pollution Prevention and Toxics (OPPT), Office of Chemical Safety and Pollution Prevention (OCSPP). file:///C:/Users/26161/Saved%20Games/Downloads/EPA-HQ-OPPT-2016-0723-0003.pdf

U.S. EPA (U.S. Environmental Protection Agency). (2017c). Toxics Release Inventory (TRI). Retrieved from https://www.epa.gov/toxics-release-inventory-tri-program/tri-data-and-tools
USGS (U.S. Geological Survey). (2002). Geohydrology, Water Quality, and Simulation of Ground-Water Flow in the Vicinity of a Former Waste-Oil Refinery near Westville, Indiana, 1997–2000. (Water-Resources Investigations Report 01-4221). Indianapolis, Indiana: U.S. Department of the Interior. https://in.water.usgs.gov/newreports/camor.pdf
WHO (World Health Organization). (2005). 1,4-Dioxane in drinking water. (WHO/SDE/WSH/05.08/120). Geneva, Switzerland.
Wissenbach, DK; Winkler, B; Otto, W; Kohajda, T; Roeder, S; Mueller, A; Hoeke, H; Matysik, S; Schlink, U; Borte, M; Herbarth, O; Lehmann, I; Von-Bergen, M. (2016). Long-term indoor VOC concentrations assessment a trend analysis of distribution, disposition, and personal exposure in cohort study samples. Air Qual Atmos Health 9: 941-950. http://dx.doi.org/10.1007/s11869-016-0396-1
Yalkowsky, SH; He, Y; Jain, P. (2010). Handbook of aqueous solubility data (2nd ed.). Boca Raton, FL: CRC Press. http://dx.doi.org/10.1201/EBK1439802458

# APPENDICES

# Appendix A REGULATORY HISTORY

## A.1 Federal Laws and Regulations

**Table_Apx A-1. Federal Laws and Regulations**

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| **EPA Regulations** | | |
| TSCA – Section 6(b) | EPA is directed to identify and begin risk evaluations on 10 chemical substances drawn from the 2014 update of the TSCA Work Plan for Chemical Assessments. | 1,4-Dioxane is on the initial list of chemicals to be evaluated for risk under TSCA (81 FR 91927, December 19, 2016). |
| TSCA – Section 8(a) | The TSCA section 8(a) CDR Rule requires manufacturers (including importers) to give EPA basic exposure-related information on the types, quantities and uses of chemical substances produced domestically and imported into the United States. | 1,4-Dioxane manufacturing (including importing), processing distribution and use information is reported under the CDR rule information about chemicals in commerce in the United States. |
| TSCA – Section 8(b) | EPA must compile, keep current and publish a list (the TSCA Inventory) of each chemical substance manufactured or processed in the United States. | 1,4-Dioxane was on the initial TSCA Inventory and therefore was not subject to EPA's new chemicals review process. |
| TSCA – Section 8(e) | Manufacturers (including importers), processors and distributors must immediately notify EPA if they obtain information that supports the conclusion that a chemical substance or mixture presents a substantial risk of injury to health or the environment. | Ten substantial risk reports from 1989 to 2004 (US EPA, ChemView. Accessed April 13, 2017). |
| EPCRA – Section 313 | Requires annual reporting from facilities in specific industry | 1,4-Dioxane is a listed substance subject to reporting requirements |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| | sectors that employ 10 or more full time equivalent employees and that manufacture, process or otherwise use a TRI-listed chemical in quantities above threshold levels. | under 40 CFR 372.65 effective as of January 01, 1987. |
| Federal Food, Drug, and Cosmetic Act (FFDCA) – Section 408 | FFDCA governs the allowable residues of pesticides in food. Section 408 of the FFDCA provides EPA with the authority to set tolerances (rules that establish maximum allowable residue limits) or exemptions from the requirement of a tolerance, for all residues of a pesticide (including both active and inert ingredients) that are in or on food. Prior to issuing a tolerance or exemption from tolerance, EPA must determine that the tolerance or exemption is "safe." Sections 408(b) and (c) of the FFDCA define "safe" to mean the Agency has reasonable certainty that no harm will result from aggregate exposures to the pesticide residue, including all dietary exposure and all other exposure (e.g., non-occupational exposures) for which there is reliable information. Pesticide tolerances or exemptions from tolerance that do not meet the FFDCA safety standard are subject to revocation. In the absence of a tolerance or an exemption from tolerance, a food containing a pesticide residue is considered adulterated and may not be distributed in interstate commerce. | In 1998, 1,4-dioxane was removed from the list of pesticide product inert ingredients because it was no longer being used in pesticide products. 1,4-Dioxane is also no longer exempt from the requirement of a tolerance (the maximum residue level that can remain on food or feed commodities under 40 CFR Part 180, Subpart D). |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| CAA – Section 111(b) | Requires EPA to establish new source performance standards (NSPS) for any category of new or modified stationary sources that EPA determines causes, or contributes significantly to, air pollution, which may reasonably be anticipated to endanger public health or welfare. The standards are based on the degree of emission limitation achievable through the application of the best system of emission reduction (BSER) which (taking into account the cost of achieving reductions and environmental impacts and energy requirements) EPA determines has been adequately demonstrated. | 1,4-Dioxane is subject to the NSPS for equipment leaks of volatile organic compounds (VOCs) in the synthetic organic chemicals manufacturing industry for which construction, reconstruction or modification began after 1/5/1981 and on or before 11/7/2006 (40 CFR Part 60, Subpart VV). |
| CAA – Section 112(b) | Defines the original list of 189 hazardous air pollutants (HAP). Under 112(c) of the CAA, EPA must identify and list source categories that emit HAP and then set emission standards for those listed source categories under CAA section 112(d). CAA section 112(b)(3)(A) specifies that any person may petition the Administrator to modify the list of HAP by adding or deleting a substance. | 1,4-Dioxane is listed as a HAP under section 112 (42 U.S.C. § 7412) of the CAA. |
| CAA – Section 112(d) | Section 112(d) states that the EPA must establish (NESHAPs for each category or subcategory of major sources and area sources of HAPs [listed pursuant to Section 112(c)]. The standards must require the maximum degree of emission reduction that the EPA determines to be | There are a number of source-specific NESHAPs that are applicable to 1,4-dioxane, including:<br>Organic Hazardous Air Pollutants from the Synthetic Organic Chemical Manufacturing Industry (40 CFR Part 63, Subpart F),<br>Organic Hazardous Air Pollutants from the Synthetic Organic |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| | achievable by each particular source category. Different criteria for maximum achievable control technology (MACT) apply for new and existing sources. Less stringent standards, known as generally available control technology (GACT) standards, are allowed at the Administrator's discretion for area sources. | Chemical Manufacturing Industry for Process Vents, Storage Vessels, Transfer Operations, and Wastewater (40 CFR Part 63, Subpart G)<br>Off-Site Waste and Recovery Operations (40 CFR Part 63, Subpart DD),<br>Wood Furniture Manufacturing Operations (40 CFR Part 63, Subpart JJ),<br>Pharmaceuticals Production (40 CFR Part 63, Subpart GGG),<br>Group IV Polymers and Resins (thermoplastic product manufacturing) (40 CFR Part 63, Subpart JJJ),<br>Organic Liquids Distribution (Non-gasoline) (40 CFR Part 63, Subpart EEEE),<br>Miscellaneous Organic Chemical Manufacturing (40 CFR Part 63, Subpart FFFF),<br>Rubber Tire Manufacturing (40 CFR Part 63, Subpart XXXX),<br>Site Remediation (40 CFR Part 63, Subpart GGGGG), and<br>Miscellaneous Coating Manufacturing (40 CFR Part 63, Subpart HHHHH). |
| Comprehensive Environmental Response, Compensation and Liability Act (CERCLA) – Sections 102(a) and 103 | Authorizes EPA to promulgate regulations designating as hazardous substances those substances which, when released into the environment, may present substantial danger to the public health or welfare or the environment. EPA must also promulgate regulations establishing the quantity of any hazardous substance the release | 1,4-Dioxane is a hazardous substance under CERCLA. Releases of 1,4-dioxane in excess of 100 pounds must be reported (40 CFR 302.4). |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| | of which must be reported under Section 103.<br>Section 103 requires persons in charge of vessels or facilities to report to the National Response Center if they have knowledge of a release of a hazardous substance above the reportable quantity threshold. | |
| Safe Drinking Water Act (SDWA) – Section 1412(b) | Every 5 years, EPA must publish a list of contaminants that: (1) are currently unregulated, (2) are known or anticipated to occur in public water systems (PWSs) and (3) may require regulations under SDWA. EPA must also determine whether to regulate at least five contaminants from the list every 5 years. | 1,4-dioxane was identified on both the Third (2009) and Fourth (2016) Contaminant Candidate List (CCL) (74 FR 51850, October 8, 2009) (81 FR 81099, November 17, 2016). |
| SDWA – Section 1445(a) | Every 5 years, EPA must issue a new list of no more than 30 unregulated contaminants to be monitored by PWSs. The data obtained must be entered into the National Drinking Water Contaminant Occurrence Database. | 1,4-dioxane was identified in the third UCMR, issued in 2012 (77 FR 26072, May 2, 2012). |
| RCRA – Section 3001 | Directs EPA to develop and promulgate criteria for identifying the characteristics of hazardous waste, and for listing hazardous waste, taking into account toxicity, persistence, and degradability in nature, potential for accumulation in tissue and other related factors such as flammability, corrosiveness, and other hazardous characteristics. | In 1980, 1,4-dioxane became a listed hazardous waste in 40 CFR 261.33 - Discarded commercial chemical products, off-specification species, container residues, and spill residues thereof (U108) (45 FR 33084). |
| **Other federal regulations** | | |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| FFDCA | Provides the U.S. Food and Drug Administration (FDA) with authority to oversee the safety of food, drugs and cosmetics. | FDA established a limit of 10 mg/kg on the amount of 1,4-dioxane that can be present in the food additive glycerides and polyglycides of hydrogenated vegetable oils (21 CFR 172.736 and 71 FR 12618, March 13, 2006). |
| Occupational Safety and Health Act | Requires employers to provide their workers with a place of employment free from recognized hazards to safety and health, such as exposure to toxic chemicals, excessive noise levels, mechanical dangers, heat or cold stress or unsanitary conditions. Under the Act, OSHA can issue occupational safety and health standards including such provisions as PELs, exposure monitoring, engineering and administrative control measures and respiratory protection. | In 1989, OSHA established a PEL for 1,4-dioxane of 100 ppm or 360 mg/m$^3$ as an 8-hour, TWA (29 CFR 1910.1001).<br>While OSHA has established a PEL for 1,4-dioxane, OSHA has recognized that many of its PELs are outdated and inadequate for ensuring the protection of worker health. 1,4-Dioxane appears in OSHA's annotated PEL tables, wherein OSHA recommends that employers follow the California OSHA limit of 0.28 ppm, the NIOSH REL of 1 ppm as a 30-minute ceiling or the ACGIH TLV of 20 ppm (8-hour TWA). |
| Atomic Energy Act | The Atomic Energy Act authorizes the Department of Energy to regulate the health and safety of its contractor employees | 10 CFR 851.23, Worker Safety and Health Program, requires the use of the 2005 ACGIH TLVs if they are more protective than the OSHA PEL. |
| Federal Hazardous Materials Transportation Act | Section 5103 of the Act directs the Secretary of Transportation to:<br>Designate material (including an explosive, radioactive material, infectious substance, flammable or combustible liquid, solid or gas, toxic, oxidizing or corrosive material and compressed gas) as hazardous when the Secretary determines that transporting the material in | The Department of Transportation (DOT) has designated 1,4-dioxane as a hazardous material, and there are special requirements for marking, labeling and transporting it (49 CFR Part 171, 40 CFR 173.202 and 40 CFR 173.242). |

| Statutes/Regulations | Description of Authority/Regulation | Description of Regulation |
|---|---|---|
| | commerce may pose an unreasonable risk to health and safety or property.<br>Issue regulations for the safe transportation, including security, of hazardous material in intrastate, interstate and foreign commerce. | |

## A.2 State Laws and Regulations

**Table_Apx A-2. State Laws and Regulations**

| State Actions | Description of Action |
|---|---|
| State PELs | California PEL: 0.28 ppm (Cal Code Regs. Title 8, § 5155). |
| State Right-to-Know Acts | New Jersey (8:59 N.J. Admin. Code § 9.1), Pennsylvania (34 Pa. Code § 323). |
| State air regulations | Allowable Ambient Levels (AAL): New Hampshire (RSA 125-I:6, ENV-A Chap. 1400), Rhode Island (12 R.I. Code R. 031-022). |
| State drinking/ground water limits | Massachusetts (310 Code Mass. Regs. § 22.00), Michigan (DEQ 2016). |
| Chemicals of high concern to children | Several states have adopted reporting laws for chemicals in children's products that include 1,4-dioxane, such as Oregon (Toxic-Free Kids Act, Senate Bill 478, 2015) Vermont (Code Vt. R. § 13-140-077) and Washington State (Wash. Admin. Code § 173-334-130). |
| Other | In California, 1,4-dioxane was added to the Proposition 65 list in 1988 (Cal. Code Regs. title 27, § 27001). |

## A.3 International Laws and Regulations

**Table_Apx A-3. Regulatory Actions by other Governments and Tribes**

| Country/Organization | Requirements and Restrictions |
|---|---|
| Canada | 1,4-Dioxane is on the Cosmetic Ingredient Hotlist as a substance prohibited for use in cosmetics. 1,4-Dioxane is also included in Canada's National Pollutant Release Inventory (NPRI), the publicly- |

| Country/Organization | Requirements and Restrictions |
|---|---|
| | accessible inventory of pollutants released, disposed of and sent for recycling by facilities across the country (Government of Canada, 2010. *1,4-Dioxane*. Accessed April 18, 2017). |
| Australia | In 1994, 1,4-dioxane was assessed. A workplace product containing more than 0.1% 1,4-dioxane is classed as a hazardous substance. 1,4-Dioxane is in Class 3, (Packing Group II) under the Australian Dangerous Goods Code (National Industrial Chemicals Notification and Assessment Scheme, NICNAS, 2013, *Dioxane (1,4-Dioxane)*. Accessed April, 18 2017). |
| Japan | 1,4-dioxane is regulated in Japan under the following legislation:<br>• Act on the Evaluation of Chemical Substances and Regulation of Their Manufacture, etc. (Chemical Substances Control Law; CSCL)<br>• Act on Confirmation, etc. of Release Amounts of Specific Chemical Substances in the Environment and Promotion of Improvements to the Management Thereof<br>• Industrial Safety and Health Act (ISHA)<br>• Air Pollution Control Law<br>• Water Pollution Control Law<br>(National Institute of Technology and Evaluation (NITE) Chemical Risk Information Platform (CHIRP), Accessed April 18, 2017). |
| Republic of Korea | The Ministry of the Environment recently adopted a provisional water quality standard for human health of 50 µg/L 1,4-dioxane in drinking water (An et al, 2014). |
| Australia, Austria, Belgium, Canada, Denmark, European Union (EU), Finland, France, Germany, Hungary, Ireland, Italy, Japan, Latvia, New Zealand, People's Republic of China, Poland, Singapore, South Korea, Spain, Sweden, Switzerland, The Netherlands, Turkey, United Kingdom | Occupational exposure limits for 1,4-dioxane (GESTIS International limit values for chemical agents (Occupational exposure limits, OELs) database. Accessed April 18, 2017). |
| WHO | Established a tolerable daily intake of 16 µg 1,4-dioxane/kg body weight based on a no-observed-adverse-effect level (NOAEL) of 16 mg/kg body weight per day for hepatocellular tumors observed in a long-term drinking-water study in rats. The WHO water quality guideline is 0.05 mg/L 1,4-dioxane in drinking water (WHO 2005). |

# Appendix B PROCESS, RELEASE AND OCCUPATIONAL EXPOSURE INFORMATION

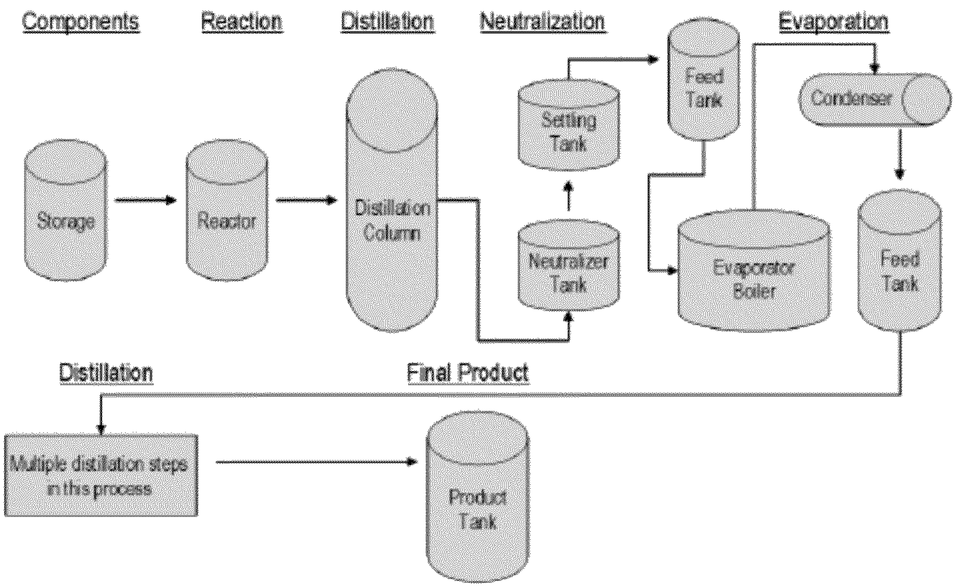
This appendix provides information and data found in preliminary data gathering for 1,4-dioxane.

## B.1 Process Information

Process-related information potentially relevant to the risk evaluation may include process diagrams, descriptions and equipment. Such information may inform potential release sources and worker exposure activities for consideration.

### B.1.1 Manufacture (Including Import)

The primary method for industrial production of 1,4-dioxane involves an acid-catalyzed conversion of ethylene glycol (mono-, di-, tri- and polyethylene glycol may be used) by ring closure in a closed system. The process is carried out at a temperature between 266 and 392°F (130 and 200°C) and a pressure between 0.25 and 1.1 atm (25 and 110 kPa). The synthesis step is performed in a heated vessel. The raw 1,4-dioxane product is then moved to a distillation column to start the purification process. Multiple steps are used to purify the 1,4-dioxane, including separation from water and volatile by-products by extractive distillation, heating with acids, salting out with NaCl, $CaCl_2$ or NaOH, and fine subsequent distillation (ECJRC, 2002). The 1,4-dioxane manufacturing plant in Zachary, Louisiana produces 1,4-dioxane using this reaction with diethylene glycol and concentrated sulfuric acid. Figure_Apx B-1 shows a process flow diagram for the process used by the manufacturer [EPA-HQ-OPPT-2016-0723-0012 (BASF, 2017)].




**Figure_Apx B-1: General Process Flow Diagram for 1,4-Dioxane Manufacturing**
Source: EPA-HQ-OPPT-2016-0723-0012 (BASF, 2017).

Two other reactions can be used to make 1,4-dioxane, but they are primarily used to make substituted dioxanes and not known to be used for industrial 1,4-dioxane production (ECJRC, 2002).

### B.1.2 Processing and Distribution

#### B.1.2.1 Processing as a Reactant/Intermediate

1,4-Dioxane can be used as a chemical reactant in the production of pharmaceuticals, polyethylene terephthalate (PET) plastics, rubber, insecticides and pesticides, cement, deodorant fumigant, magnetic tape and adhesives [EPA-HQ-OPPT-2017-0723-0003 (U.S. EPA, 2017b)]. Exact process operations involved in the use of 1,4-dioxane as a chemical reactant are dependent on the final product that is being synthesized. For the use of 1,4-dioxane as a chemical reactant, operations would typically involve unloading 1,4-dioxane from transport containers and feeding the 1,4-dioxane into a reaction vessel(s), where the 1,4-dioxane would react either fully or to a lesser extent. Following completion of the reaction, the produced substance may or may not be purified further, thus removing unreacted 1,4-dioxane (if any exists). Reacted 1,4-dioxane is assumed to be destroyed and is thus not expected to be released or cause potential worker exposures.

#### B.1.2.2 Processing – Non-Incorporative

1,4-Dioxane is used as a process solvent during the manufacturing of cellulose acetate, resins, waxes and fats [EPA-HQ-OPPT-2017-0723-0003 (U.S. EPA, 2017b)].

#### B.1.2.3 Repackaging

Typical repackaging operations involve transferring of chemicals into appropriately sized containers to meet customer demands/needs.

#### B.1.2.4 Recycling

1,4-Dioxane is used as a solvent in several applications. In this capacity, 1,4-dioxane can be regenerated and recycled for reuse.

### B.1.3 Uses

#### B.1.3.1 Processing Aids, Not Otherwise Listed

Processing aids are chemical substances used to improve the processing characteristics or the operation of process equipment or to alter or buffer the pH of the substance or mixture, when added to a process or to a substance or mixture to be processed. Processing agents do not become a part of the reaction product and are not intended to affect the function of a substance or article created (U.S. EPA, 2016a). 1,4-Dioxane is used in a number of industrial processes as a processing aid. These processes include wood pulping, extraction of animal and vegetable oils, textile processing, polymerization, pharmaceutical purification and etching of fluoropolymers [EPA-HQ-OPPT-2017-0723-0003 (U.S. EPA, 2017b); EPA-HQ-OPPT-2016-0723-0012 (BASF, 2017)]. Exact process operations involved in the use of 1,4-dioxane as a processing aid are dependent on the final product that is being synthesized.

#### B.1.3.2 Functional Fluids (Closed System)

Functional fluids are liquid or gaseous chemical substances used for one or more operational properties (U.S. EPA, 2016a). 1,4-Dioxane is used in polyalkylene glycol lubricants, synthetic metalworking fluids, cutting and tapping fluids and hydraulic fluids [EPA-HQ-OPPT-2017-0723-0003 (U.S. EPA, 2017b)]. Exact operations involved in the use of 1,4-dioxane as a functional fluid are dependent on the final product.

#### B.1.3.3 Laboratory Chemicals

1,4-Dioxane is used in laboratories as a chemical reagent, reference material, stable reaction medium, liquid scintillation counting medium, spectroscopic and photometric measurement, cryoscopic solvent and histological preparation [EPA-HQ-OPPT-2017-0723-0003 (U.S. EPA, 2017b)]. Laboratory procedures are generally done within a fume hood, on a bench with local exhaust ventilation or under general ventilation.

#### B.1.3.4 Adhesives and Sealants

1,4-Dioxane is found in film cement and as a residual contaminant in two-component glues and adhesives [EPA-HQ-OPPT-2017-0723-0003 (U.S. EPA, 2017b)]. The application procedure depends on the type of adhesive and the type of substrate. After the adhesive is received by the user, it may be diluted or mixed prior to application. The formulation is then loaded into the application reservoir or apparatus and applied to the substrate via spray, roll, curtain or syringe or bead application. Application may be manual or automated. After application, the adhesive or sealant is allowed to dry, usually at ambient temperature, such that the solvent completely evaporates and a bond is formed between the substrates (OECD, 2015).

#### B.1.3.5 Other Uses

Other conditions of use where 1,4-dioxane may be formulated into a product or used as part of another process may include use in fuels and fuel additives [EPA-HQ-OPPT-2016-0723-0012 (BASF, 2017)], spray polyurethane foam and in printing and printing compositions [EPA-HQ-OPPT-2017-0723-0003 (U.S. EPA, 2017b)].

### B.1.4 Disposal

1,4-Dioxane is disposed of to a variety of environmental media: land, water and air. Land disposals include Class I underground injection, RCRA Subtitle C landfills and to other uncategorized land points. 1,4-Dioxane is sometimes discharged to water. Wastewater treatment may or may not precede these water releases. Additionally, 1,4-dioxane is also commonly incinerated (U.S. EPA, 2017c).

## B.2 Occupational Exposure Data

EPA presents below an example of occupational exposure-related information from the preliminary data gathering. EPA will consider this information and data in combination with other data and methods for use in the risk evaluation.

Table_Apx B 1 summarizes OSHA CEHD data by North American Industry Classification System (NAICS) code (OSHA, 2017a, b).

**Table_Apx B-1. Summary of Industry Sectors with 1,4-Dioxane Personal Monitoring Air Samples Obtained from OSHA Inspections Conducted Between 2002 and 2016**

| NAICS | NAICS Description |
|---|---|
| 315225 | Men's and Boys' Cut and Sew Work Clothing Manufacturing |
| 325199 | All Other Basic Organic Chemical Manufacturing |
| 334418 | Printed Circuit Assembly (Electronic Assembly) Manufacturing |
| 336399 | All Other Motor Vehicle Parts Manufacturing |
| 926150 | Regulation, Licensing, and Inspection of Miscellaneous Commercial Sectors |